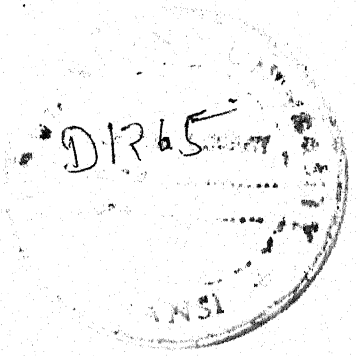
ROLE OF CALCIUM AND IRON IN AETIOLOGY AND MANAGEMENT OF ORAL SUBMUCOUS FIBROSIS

Thesis For

MASTER OF SURGERY

(OTORHINOLARYNGOLOGY)



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Certificate

This is to certify that present work entitled **"Role of Calcium and Iron In Aetiology and Management of Oral Submucous Fibrosis"** is based on the observations of ***Dr. Rajeev Kumar,*** Resident in the Department of Otolaryngology, M. L. B. Medical College, Bundelkhand University, Jhansi and has been undertaken by him under my personal supervision and guidance. It is being forwarded for evaluation as a part of requirement for appearing in M.S. (ENT) Examination of the Bundelkhand University.

Dated : November, 2000

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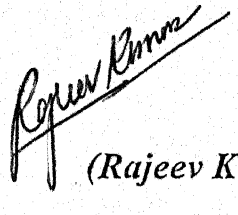

(Rajeev Kumar)

Contents

Introduction

Oral Submucous fibrosis is not an unknown clinical entity from the era of SUSRUTA, who described a clinical condition similar to it and named VIDARI. Schwartz first reported this disease in modern literature, workers suggested different name for this disease based on the observations and clinical resemblance to other diseases. Joshi coined the present and widely accepted name "Oral Submucous Fibrosis" in 1953. Apart from being reported mainly from India it has also been diagnosed in Ceylon, Malaysia, Nepal, South Vietnam and Thailand by Pindborg (1966). Joshi (1953) reported a peculiar blanching sclerosis of the palate and pillars of the faucies in some of his Indian patients. Su (1954) described his findings in three cases of "Idiopathic Scleroderma of the Mouth" and earlier Schwartz (1952) reported a case of "Atrophia Miopathica Mucosae Oris" occurring in Indians in East Africa. He had seen five such cases in 10 years, all of them in Indian woman in East Africa. Other names that have been suggested for this disease entity are "Idiopathic Scleroderma of the Mouth" by Su (1954), "Idiopathic palatal fibrosis' by Rao (1962) and "Sclerosing Stomatitis" By Wahi et al (1962). Though the more appropriate name of this disease would be "Juxta Epithelial fibrosis" but the term "Oral Submucous Fibrosis" is continuing in the literature.

The Aetiology of submucous fibrosis is uncertain and has been a subject of considerable speculation. In the Indian of the custom of chewing the nut of Areca catechu (betelnut) often combined with piper betal leaf, slaked lime, tobacco and powdered catechu in the form of 'Pan' has lead to the assumption that the "Betel Habit" is the cause of Oral Submucous Fibrosis. However the innumerable number of people who chew betel do not have Oral Submucous Fibrosis while many others are afflicted with this condition have never used betel (De Sa, 1957, Pindborg and Singh 1964). On the evidence of animal experiments Sirsat and Khanolkar (1962) believe that the betel chewing does not cause Oral Submucous Fibrosis. The epidemiological survey of Lemmer and Shear (1967) among South African Indians suggested that there might be positive relationship between betel nut chewing and the onset of the disease. Other local irritants suggested as possible aetiological factors while certain features of the condition suggest an Allergic origin, Autoimmune disorder, Intermediate Stage of Malignant transformation or a relationship to collagen disease (Su, 1954; De Sa, 1957; Sirasat and Khanolkar, 1957; Rao 1962; Pindborg and Singh, 1964). Oral Submucous Fibrosis is the disease of increasing incidence in our country, particularly in Eastern Uttar Pradesh, since the tobacco and betel chewing is commonly practiced in this region. Due to increase incidence it attracted the attention of clinicians in aetiopathogenesis to establish the management of the disease in this Area. This statement is highlighted by the fact that full session on Oral Submucous

Fibrosis was scheduled in 41st Annual Conference of Association of Otolaryngologists of India held at Mysore (2 to 6 Jan, 1989). The management of Oral Submucous Fibrosis is as uncertain as its aetiology, various forms of treatment have been advocated including local injections of steroid and Hyalase, Antioxidants, multivitamins, microneutrients and surgical approach in removal of fibrous bands but the main problem with any mode of treatment has been the recurrence of symptoms after some months mainly trismus, inability to open mouth and protrude tongue, intolerance to Hot Spicy food & Chillis, inability to blowout candle or inability to whistle symptoms appear after some months. The present study was, therefore carried out with the following aims and objects.

1. *To Study prevalence of Oral Submucous Fibrosis in Bundelkhand.*
2. *To study the clinical profile of patients of Oral Submucous Fibrosis.*
3. *Role of Calcium and Iron in Aetiology of Oral Submucous Fibrosis.*
4. *Role of Calcium and Iron in Management of Oral Submucous Fibrosis.*
5. *Evaluation of different methods of treatment of Oral Submucous Fibrosis.*

This research might help to find out the cause and the effective management of Oral Submucous Fibrosis.

REVIEW OF LITERATURE

Review of Literature

In the present era, the oral Submucous fibrosis drawn the attention of clinicians in the early fifties. However if we refer back to our ancient history of Indian Medicine, this disease was first described by SUSRUTA. In the classification of mouth and throat meladies, he mentioned a condition called "VIDARI" whose features were progressive narrowing of mouth, depigmentation of oral mucosa and pain while taking food. The same features precisely fit into modern clinical condition, oral submucous fibrosis (Shastri, 1924).

In modern era of medicine, clinicians came into consideration of this clinical entity from sixth decade of the current century. It was Schwartz (1952) who first described the disease as 'Atrophica Idiopathica (Tropica) Mucosae Oris'. He found the disease in five ladies of Indian origin in East Africa and Kenya. One year later Joshi (1953) described the same clinical condition, reporting 41 cases from India and it was Joshi who coined the term 'Submucous Fibrosis'.

Informations obtained from many part of the world lead to the believe that, this submucosal dyscrasia is particular to the people of Indian origin. But Su (1954) reported three cases from China (Taiwan) and showed its occurrence in different

population groups. Rao (1954) also found oral submucous fibrosis in some Europeans, living in Hyderabad. Turner (1966) found a typical case of Oral Submucous Fibrosis in an English woman married to a Pakistani individual in England. Lalchand (1962) reported 15 cases from Nepal during his visit for 25 days. Pindborg (1964) observed similar condition in two Danish patients also. Beside a few cases of other than Indians, it is of general belief that the disease is commonly found in Indian subcontinent or in persons of Indian origin settled abroad.

In 7th decade, multifactorial study was performed by Pindborg and associates (1962, 1964, 1966 and 1968) covering the aspects, epidemiology and geographical distribution to pathology and clinical behavior. Later on workers concentrated themselves on the pathogenesis and management of the disease.

Definition: -

The oral submucous fibrosis was defined by Pindborg et al. (1966). "An insidious, chronic diseases affecting any part of the oral cavity and sometimes the pharynx. Although occasionally preceded by vesicle formation, it is always associated with Juxta-epithelial inflammatory reaction followed by a fibroelastic change of the lamina propria with epithelial atrophy leading to stiffness of oral mucosa causing trismus and inability to eat'.

Geographical Distribution: -

Before the works of Pindborg et al. (1962), the disease was reported in Indians only, except few cases reported by Su (1954), Rao (1954). Some Europeans, suffering from this disease, living in Hyderabad, were reported by Rao (1954). Su (1954) reported oral submucous fibrosis in three Chinese. In early fifties first report came from Schwartz (1952) who described it in five Indian women from Africa and Kenya. He also reported one Indian student from Ugenda and an English lady married to a Pakistani person. Pindborg (1962) reported two Danish patients having same clinical presentation. On his visit to Sri Lanka, Malaysia, Nepal, Thailand and South Vietnam, Pindborg (1964) saw a number of cases of oral submucos fibrosis. Shiau and Kwan (1979) reported 35 cases of oral submucous fibrosis from Taiwan. Laskaris, et al. (1981), described an unusual case of Non-Indian having oral submucous fibrosis. She was a sixty two years old Greek female.

Inspite of these reporting, it is now well accepted that oral submucous fibrosis is a disease of Indian sub continent and mainly occurs in populations of Indian origin. Most of the cases, reported out side of south East Asia i.e. from Europe and Africa, were migrated Indians.

In our country the disease is not having a definite trend of distribution but having slight predominance in Southern India as compared to Northern India (Pindborg, 1964). In Southern part, maximum number of cases have been reported

from Kerala and Andhra Pradesh. Pindborg (1964) studies the prevalence of disease and found that the incidence was more in Kerala, Andhra Pradesh, Tamilnadu, Eastern Uttar Pradesh and Bihar. Sirsat and Khanolakar (1962) reported large number of cases in Bombay. Yadav (1978) reported many cases from Eastern Uttar Pradesh and Bihar. Varghese et al. (1985), Bhonsle et al (1987) found that the disease is more prevalent in cashew workers of Kerala.

Incidence & Prevalence :

Oral Submucous fibrosis has been reported as a pathological entity in several studies from India (Pindborg et al. 1966, 1964) De'Sa (1957;) Joshi, (1953) and from abroad (Su, 1954) and Shiau, (1979) etc. It is an uncommon lesion which is confined to the oral mucosa and which is remarkable because it is found almost exclusively in Indians (Hammer and Shear et al. 1967). Possible exceptions are three cases from Formosa reported by Su (1954) who does not report the race of the patients and some 'Europeans' reported in 1962 by Rao.

Oral submucous fibrosis is a recognized and documented precancerous lesion. It occurs at an earlier age than the other oral precancerous lesions.

Submucous fibrosis as a condition was first described in the Indian medical literature just over 52 year's age by Schwartz (1952). Since then it has been recorded occasionally under different names, but Pindborg et al in 1964 suggested that 1 in 1600 of the Indian population might be affected by this disease. All the recorded cases

have involved Indians apart from a few Asians and Europeans living in India and a recent case of a white South African woman reported by hammer and Shear (1967).

Age group falling between 20 and 40 years (Simpson, 1968) is slightly more susceptible, Rao from Hyderabad (1962) has reported 46 patients of this disease. In his series, most patients were in Second decade of life, the youngest being 12 years old and the eldest 64 years, 17 were men against 29 woman indicating a higher incidence amongst the females. Submucous fibrosis occurs more frequently than hitherto assumed. Recent epidemiological studies in Lucknow and Bombay in India, have shown a frequency of about 0.5 percent (Pindborg, 1965). It has been reported mainly from India but has also been diagnosed in Ceylon, Malaysia, Nepal, South Vietnam and Thailand by Pindborg (1966).

Epidemiological studies on the prevalence of submucous fibrosis have been done by Pindborg et al and shear et al. (1967). Pindborg et al (1963) and Zacharian et al. (1966) examined 35000 urban Indians seeking admission to Clinics at dental colleges in Lucknow, Bombay, Banglore and Trivandrum and found the following prevalence figures respectively 0.5%, 0.5%, 0.2% and 1.2% Shear et al. (1967) who examined 1000 Indians in South Africa found a prevalence of 0.5%.

In 1962 Sirsat and Khanolkar reported age wise distribution in three series of submucous fibrosis of the palate in Bombay as seen in table No. 1.

Table No. 1

Series	No of cases	Age group in Years					
		1-10	11-20	21-30	31-40	41-50	51-60
I	41	-	2	20	11	6	2
II	64	2	11	27	17	8	1
III	85	2	12	32	26	10	2

The disease appears to have started in only four persons during the first ten years of life, whereas the majority of the patients belonged to the 20 to 40 age group.

In 1956 Pindborg reported 40 cases of oral submucous fibrosis with oral cancer with their sex and age distribution as seen in Table No. 2

Table No. 2

Sex	Age group in years					Total
	20-29	30-39	40-49	50-59	60-69	
Male	2	-	5	10	11	28
Female	-	1	-	10	1	12

In 1968 Pindborg reported age distribution in 63 patients of oral submucous fibrosis, as shown table No. 3.

Table No. 3

Sex	Age group in years							Total
	20-29	30-39	40-49	50-59	60-69	70-79	80-89	
Male	-	1	6	3	5	1	-	16
Female	3	12	11	12	7	1	1	47
Total	3	13	17	15	12	2	1	63

The youngest patient was 22 years old and the oldest was of 84 years, the peak frequency was between the ages of 40 and 60 years, the peak frequency was between the ages of 40 and 60 years. Females were more in number than the male patients.

In 1979, Shisu and Kwen reported age distribution in patients of oral submucous fibrosis in Taiwan as per details in table no. 4

Table No. 4

Sex	Age group in years						Total
	10-19	20-29	30-39	40-49	50-59	60-69	
Male	2	6	10	8	6	2	34
Female	0	0	0	0	0.	1	1
Total	2	6	10	8	6	3	35

In the above report the youngest patient was 17 years old and the oldest was of 64 years. The peak frequency was between the ages of 30 and 50 years. Male patients were more (97%) than female patients (3%).

Paymaster (1956) in study of buccal mucosa in 650 Indian patients found that younger persons were commonly affected by oral submucous fibrosis. Pindborg (1964) reported submucous fibrosis in an eight-year-old boy of Indian origin from Singapore. The youngest case was from India. She was an Indian girl aged four years, reported by Hayes (1985).

Information obtained from many parts of the world leads up to the belief that oral submucous fibrosis is peculiar to the people of Indian origin, although it was first reported in East-Africa by Schwartz, 1952.

Table No. 5: - Showing geographical distribution of oral submucous fibrosis in world.

Investigator	Year	Country	Age range	Peak age
Schwartz	1952	E. Africa	-	-
Lal	1953	India (M.P.)	-	-
Joshi	1953	India (Bombay)	-	40-60
Su	1954	China	-	30-40
Rao & Raju	1954	Nepal	18-40	-
De'Sa	1957	India (Bombay)	19-55	-
Sharan	1957	India (Bihar)	13-62	-

Rao	1962	India (Hyderabad)	12-64	-
Sirsat & Khanolkar	1962	India (Bombay)	10-58	20-40
Pindborg	1966	India	22-77	44-50
Pindborg	1968	India	22-84	40-60
Shishu	1979	Taiwan	17-64	32-50
Present study	2000	India (Jhansi)	10-60	20-30

The above table indicates that oral submucous fibrosis has chiefly Involved with age group of 35-40 years.

The less ratio of incidence reported by (Wahi & Su, Wahi and associates), was 2:1 male to female and all of the three cases presented by Su involved male patients. However Joshi (1953), De'Sa 91957) and Sirsat and Khanolkar (1962) reported more than 50 percent female victims.

Religion :

In India, the shaping of castes and communities is governed not only by the geographical location but also by their religion and language. Different communities resident in the same geographical area acquire different and divergent habits of living, such as those pertaining to (1) Nutritional Practices (2) Marriage Customs (3) Hygienic observations. It is a well established tenet of epidemiology that the etiology of disease can often be sought with success in the habits of the people. An analysis of

the incidence of submucous fibrosis of the palate was carried out by Sirsat and Khanolkar (1962) in 190 cases in Bombay as shown in Table No. 6.

Table No : 6

Series	No. of cases	Communities				
		Hindus	Parsi	Muslims	Christian	others
I	41	34	-	2	5	9
II	64	42	3	5	3	11
III	85	57	3	5	2	18

Aetiological Factors :

The exact causes of submucous fibrosis is obscure. The various hypothesis put forward so far suggest a multifactorial origin for this condition. Along side the role of local irritants such as capsicum (Sirsat SM, Khanolkar VR 1960), Tobacco (paymaster JC 1956), Areca nut(Canniff JP, Harvey W, 1981), pungent & spicy foods (Pindborg JJ, Sirsat SM) and alcohol (Wahi P. N. et al. 1966), an underlying systemic predisposition is likely because of the geographical and ethnic distribution of OSMF.

Among systemic factors the main ones incriminated are chronic iron and vitamin B-Complex deficiency, anaemia (Rajendran R et al 1990) and a genetic predisposition to the disease (Canniff JP et al. 1986).

1. Local Factors :

In the pathogenesis of submucous fibrosis might lie the continuous prolonged action of mild irritants. Since the disease occurs predominantly among Indians a possible allergen has been suspected in their common diet. Spices being an essential ingredient in Indian diet, would attract attention, especially chilli papers, which are universally used in all parts of India. Support for this theory that chillies are the irritating factor is found in the occurrence of submucous fibrosis among Indians living out side India but maintaining Indian dietary habits. A number of cases of submucous fibrosis have been diagnosed in such countries as Ceylon, Nepal, Thailand and South Vietnam where chillies are commonly used in the diet. Sirsat and Khanolkar (1960) demonstrated changes similar to human submucous fibrosis after painting palate of the rat with chillies lotion.

Chronic irritation has been thought to be the local factor to induce the pathological changes in the oral mucosa. Among the possible irritants, tobacco, liquor, chillies and betel nut have been regarded the most important causative agents.

In the study of Shisu (1979), involving patients of submucous fibrosis 5 were liquor users, 18 were smokers and 21 were betel nut chewers. In this study betal nut chewing was more common in-patients of oral submucous fibrosis. The history of betal nut chewing among in twenty one patients was varied. The duration ranged from

as long as 20 years or more to as little as 1 year before submucous fibrosis was clinically diagnosed.

According to Su (1954) the mode of action of betel nut over the buccal mucosa could be a continuous and prolonged action of an alkeloid, Arecoline, on the nerve endings in the oral mucosa with consequent neurotrophic disorder of the area.

According to Pindborg (1965) the most important etiological factors for producing oral submucous fibrosis and oral cancer are tobacco and betel nut. In his study on 40 patients of oral submucous fibrosis and oral cancer, all patients except one, had the habit of consuming tobacco mixed with betel nut and lime, Sinha (1980) reported the presence of oral submucous fibrosis is more in those areas where the habit of consuming tobacco in prevalent. This fact also suggests that consumption of tobacco is an etiological factor for oral submucous fibrosis.

Betel and Betel Nut:

The habit of chewing of betel nut is very common practice in India. Betel nut is either taken alone or in the form of PAN & GUTKIIA. PAN is a preparation of betel leaf, betel (Areca) nut (raw or crushed), slaked lime and catechu. It may or may not be combined with tobacco. The bolus, formed by chewing the preparation is swallowed, spat or kept in the mouth for some time even during sleep. Bolus of PAN is usually kept in lower buccal sulcus.

Khaini (Tobacco Chewing)

Khaini is a common practice among Indians. Bolus of pieced raw tobacco leaves are mixed with lime and it is kept in lower labial or buccal sulcus. Though the Khaini habit is common in rural and urban both, it has slight predominance among the rural population.

Gutkha:

This rank first in local factors. This is commercially powder containing betel nut, tobacco and catechu, preservative with certain chemical ingredient (e.g. leather tinning agent). Gutkha is most commonly used local irritant factor in all over India, mainly in Bihar, Uttar Pradesh, Madhya Pradesh, Rajasthan, Maharastra. This is easily available in attractive pouches containing about 5 to 10 grams of commercial powder. Few companies use various types of chemicals (e.g. Gambiar) instead of catechu because these chemicals are cheaper. These chemicals are more irritant to buccal mucosa.

Smoking:

Although Cigarette smoking is common all over the world Bidi, Chutta, Chilam are smoked in Indian sub continent only. Bidi is a locally made cigarette prepared by tobacco (0.30-0.36 gm.) rolled in Tendu leaves. Chutta is a preparation similar to Bidi and practiced in Tamilnadu. In some regions of Andhra Pradesh, reverse smoking (keeping burning end inside the mouth) is commonly done. Chilam is another method

of smoking, which is done with the help of a conical clay pipe of about 10cm in length. It is smoked from its narrow end keeping a piece of cloth covering it. Wider end is filled either with tobacco or with cannabis. The wider end is flamed before smoking and the cotton serves as filter.

Hokka :

It is an Indian pipe. Upper end of hokka is attached to Chilam, described above, but the material being smoked, is always tobacco (not the cannabis). In hokka the smoke is filtered through the water before reaching to smoker. It is commonly found in every rural home of Northern India.

Spices and Chillies:

Spices are the essential ingredients of Indian foods. Almost all of the Indian food preparations are spiced. The choice of preparation may differ but the spices are invariably used. Most of the Indians are very fond of chillies too. Spices and chillies both act as continuous irritants to oral mucosa when they are used for prolonged period. Beside the smoking and food habits, oral hygiene and nutritional status of patients play an important role in the development of the disease process. Pindborg (1964) quoted poor oral hygiene in most of the patients observed by his team. Sirsat and Khanolkar (1962) observed that majority of the patients was under nourished.

Rajendran et al. (1986) working on cell mediated and humoral response in oral submucous fibrosis, came to conclusions of disease being an autoimmune disorder.

Seedat et al. (1988), in their recent work on oral submucous fibrosis were off the opinion of genetic predisposition, playing an important role in the development of the disease.

2- Blood Chemistry and Haematological Variations:

Rajendran R et al (1990) stated that the deficiencies of vitamin B12 folate and Iron can affect the integrity of the oral mucosa.

Significant haematological abnormalities have been reported in Oral Submucous fibrosis, including an increased blood sedimentation rate (ESR), anaemia & eosinophilia (Pindborg JJ. Sirsat SM 1966).

A significant depression of the lactate dehyrogenase isoenzyme ration (LDHIV/LDH II) is reported at the tissue level in Oral Submucous fibrosis. A significant reduction in the serum copper and zinc ratio is also reported (Varghese I et al. 1987).

Decreased Serum Zinc and Iron level are also reported as Bioindicators of precancerous nature of Oral Submucous Fibrosis. (Paul et al 1996).

Role of multiple micronutrients Supplementation in the management of Oral Submucous Fibrosis is carried out in Karachi, Pakistan. (Maher R, et al 1997)

A study of Serum protein, ascorbic Acid, Iron & tissue Collagen in Oral Submucous Fibrosis (Anuradha CD, Devi CS 1993, and Rajendran R, Vasudevan DM 1990). Showed altered Serum ascorbic acid, iron, protein & tissue collagen levels.

3- AutoImmunity:

Canniff JP et al in 1986 reported high incidence of anti nuclear antibodies together with autoanti bodies to gastic parietal cells, thyroid microsomes, reticulin and smooth muscle in Oral Submucous Fibrosis.

The increased frequency of HLA halotypic pairs A 10/DR3 B8/DR3 and A 10/B8 in OSMF and scleroderma suggets on MHC mediated immunological derangement operating in this disease.

4- Cytogenetics:

Ghosh P. K. et al (1990) stated that sister (?) chromatid exchange (SCE) levels are raised in the peripheral blood of patients with Oral Submucous Fibrosis. This may be attributed to the genotoxic effect of the constituents of betal nut.

Clinical Features:

The onset of oral submucous fibrosis is incidious. It usually spreads over a period of years. In most of the observations, the earliest symptom was burning sensation which made the eating of spicy food, painful and difficult (Paymaster, 1956 and Pindborg et al, 1964). Pindborg (1968) described blistering and ulceration of oral mucosa and recurrent stomatitis as early symptoms. There after a variety of symptoms may appear. Su (1954) and DeSa (1957) described trismus being commonest symptom of oral submucous fibrosis, followed by tightness and loss of elasticity of oral mucosa. This fibrosis spreads to submucosal layer and involves underlying

muscle layer. If pharyngeal muscles are involved, it causes ankyloglossia. Severely affected palate produces symptoms of nasal speech and nasal regurgitation.

Rao (1962) found earache associated with oral submucous fibrosis when pharynx was involved in the disease process. This might lead to deafness, depending upon degree of involvement of pharyngotympanic tubes. In his observation, the commonest affected sites were palate and pillars of fauces. The buccal mucosa and tongue were also involved frequently.

Paymaster (1957) observed that the typical appearance of affected buccal mucosa was lusterless and pearly white. This condition was progressive to a dull white appearance of mucosa with areas of band of scar tissue, giving a reticular pattern. These patterns were best seen along the edge of soft palate. There was contraction of uvula also. Soft palate became hard and immobile. The immobility (or reduced mobility) of the palate resulted into nasal voice and nasal regurgitation. In the patients having prolonged history of disease, the reticular pattern of fibrous spread lead into the pillars of fauces and posteriorly into pharynx. Sometimes this spread was more extensive, even covering pyriform fossa. Buccal mucosa was showing same appearance of fibrous band and further spread occurred towards lips (Bhatt 1986). There was often atrophy of the papillae and appearance of patchy baldness of the dorsum of tongue (Soni et al., 1981). The lingual sulcus appeared to be lost if the floor of mouth became involved.

Soni et al. (1981) also reported the loss of taste papillae and presence of patchy baldness of tongue. After doing elctrogustometery, they found some degree of impairment of taste sensation in 24% cases. They emphasised atrophy of taste buds as possible cause of impairment of taste in oral submucous fibrosis. They classified the disease into four categories based on observation of electric gustometery.

Sl. No.	Severity of the disease	Electrogustometric observations
1.	Mild	50 - 100 uA
2.	Moderate	100 - 200 uA
3.	Severe	200 - 300 uA
4.	Eugesia	above - 300 uA

Classifications:

Depending upon severity and extension of disease. DeSa (1957) classified oral submucous fibrosis into three stages.

Stage I : (Early Stage)

It is an early stage of the disease where the patients complaint of fibrotic bands. There is no trismus and Tongue is not invoved (no ankyloglossia).

Stage II : (Established Stage)

In this stage patients complaint of trismus along with the presence of fibrotic bands. Tongue is involved but not grossly.

Stage III : (Advanced Stage)

In third stage of oral submucous fibrosis, there is gross involvement of tongue resulting ankyloglossia along with severe trismus. Palpable fibrotic bands are also present.

Rao (1962), after series of studies on oral submucous fibrosis put following symptoms forward, covering most of the clinical features of the disease.

1. *Inability to open mouth.*
2. *Inability to take pungent food and intolerance to chillies.*
3. *Inability to blow out candle or inability to whistle.*
4. *Inability to protude tongue.*
5. *Pain in the ears.*
6. *Swelling and pain around the lower jaw & neck.*

Inability to Open the Mouth:

In very early stage, the disease remains asymptomatic completely. Whitish appearance of the palate due to fibrosis is limited to soft palate. The blanching appearance of soft palate and fibrosis is being diagnosed accidently during the examination of patients for some other disease. It the condition is overlooked, over a period of years (usually two to three) patients develop inability to open mouth. This inability leads to clinical condition called trismus. It is the stage of trismus when

patients first report to otolaryngologist. The other associated findings at this stage may be as follows :

a) *Trismus being so severe, leads to progressive narrowing of mouth opening. The average distance between upper and lower incisors may be reduced to 4-6 mm. The patient maintains his nutrition with great difficulty because his ability of taking food is reduced to semisolid and liquids only.*

b) *The soft palate becomes whitish and arched. The fibrosis extends to the buccal area on both sides. It is extent and contraction of the fibrous tissue, underneath the mucosa, over the inter alveolar region and behind molar and pterygomandibular raphe, which produce trismus.*

c) *The fibrosis progresses to the lateral wall of pharynx via the pillars and it may extend down to the pyriform fossa. The uvula may become small and contracted due to fibrosis. The cheek, when palpate bimanually from outside with support of fingers inside of oral cavity, gives impression of tough feeling and increased thickening. The soft palate showes restricted mobility and has hard rubbery feel. Some times the restricted mobility results into nasal speech and regurgitation.*

Inability to Take pungent Food:

As the disease advances, the patients becomes unable to tolerate pungent hot

food. The problem becomes more severe when the foods are spicy and seasoned with chillies (Capsicum anvum and Capsicum frutescus). In fact intolerance is the first symptom in many cases, which is followed by trismus after few months. It is believed that the fibrosis is the natural outcome of the continuous prolonged irritation of oral mucosa (Pindborg et al, 1964).

Inability to Blow out Candle or Inability to Whistle:

It is a qualitative evaluation of the fibrosis and movement of tongue, cheek and palate together. Patients of oral submucous fibrosis, are usually unable to blow a candle out at a distance where normal individual can do so (aprox. Half feet) or unable to whistle. It is due to severity of fibrosis, producing hard and immobile cheeks, palate and tongue. Though the palate is as fibrosed as cheek (or some time more fibrosed) yet its mobility is maintained up to some degree and nasal regurgitation and nasal speech are resulted only in very advanced cases of oral submucous fibrosis.

Inability to Protrude Tongue:

This symptom develops when the contracting fibrosis extend to the tongue. Severe fibrosis involves the muscular layers and reduced the mobility resulting ankyloglossia. Some time baldness of tongue is also seen (Soni et al, 1978). Which results in taste impairment.

Pain in the Ears :

It is a referred symptom, presented when pharyngeal fibrosis occurs. Severe fibrosis to this area may result in contraction and scarring of Eustachian tube opening, causing conductive deafness in some cases of oral submucous fibrosis.

Swelling & Pain Around Lower Jaw and Necks:

Continuous trismus is bound to affect oral hygiene. It may lead to ulceration in oral mucosa. Due to ulcers, infections and reduced hygiene, pain and swelling may develop around the jaw and neck. This symptom is presented in very advanced stage of the disease (Pindborg et al, 1954 an Sirsat et al, 1962).

Investigations:

Various investigations have been tried but none found to be diagnostic. Pindborg et al. (1964) found mild iron deficiency anaemia in 40% of the patients. They also noted mild neutropenia. Percentage of anaemia patients in oral submucous fibrosis was even higher (Sirsat and Khaolkar, 1962). Rao (1962) and Sirsat & Khanolkar (1962) found eosinophilia in most of the cases of oral submucous fibrosis. These observations were confirmed by Mukherjee and Biswas (1972) and Phatak (1978). Erythrocyte sedimentation rate (ESR) was found raised in most of the cases (Rao, 1962), Sirsat & Khanolkar, 1962, Pindborg et al. 1964 Mukherjee and Biswas, 1972 and Phatak, 1978).

Rao (1962) studied bone marrow spectrum in-patients of Oral Submucous fibrosis. His findings were suggestive of picture of an allergic reaction, marrow being hypercellular and eosinophilic. These were negative for L E Cells. Urine and gastric tests too were non-contributory (Rao, 1962).

Mukherjee et al. (1972) conducted series of investigations to establish diagnosis of oral submucous fibrosis. They found that there was significant elevation of serum mucoproteins and serum mucopolysaccharides. According to him these elevations represented the reactions in active stage of disease, where breakdown of tissue and degeneration of collagen were taking place.

ASO titre was measured by Mukherjee et al. (1972) showed its rise in all cases. They concluded that immunologic reponse in the form of loclaised collagen disorders was responsible for the disease. Phatak (1978), analysing serum proteins and immunoglobulins in oral submucous fibrosis, agreed with the results of Mukherjee et al (1972). In his observations, he found that in oral submucous fibrosis :

1. *Total proteins were elavated as compared to control.*
2. *Total globulins were elevated.*
3. *Total immunoglobulins were significantly elevated.*
4. *The fraction, which showed elevation in immunoglobulins, was IgG.*
5. *IgA fraction was unaltered.*
6. *IgM fraction did not show any alternation.*

Phatak (1979), in another study of fibrin factors, found that there was a strong fibrin precipitating factor present in the saliva of the patients of oral submucous fibrosis. Plasma fibrinogen levels were elevated. Precipitable fibrinogens were also noted.

Immunological studies performed so far, suggested an increase in Null cells population (Phatak, 1979), hyperglobunaemia (Magdun, 1970, Mukherjee et al, 1972) and increase in mononuclear cells observed in microscopic study of fibrous tissue (Phatak and Gosavi, 1975, Adhvanu, 1986)

Gupta et al. (1985) estimated major immunoglobulin profile by immunodiffusion. They observed that severity of oral submucous fibrosis was directly proportional to estimated elevated level of major immunoglobulins. This may be a pointer to know the gravity of disease.

Rajendran et al. (1986) assessed cell mediated and humoral responses in oral submucous fibrosis. The number of high affinity rosette forming cells (ARFC) was found significantly decreased in oral submucous fibrosis and oral cancer. Where as the number of total rosette forming cells (TRFC) remained unaltered, levels of serum IgA, IgD and IgE were found elevated both in oral submucous fibrosis and in oral cancer.

Varghese et al. (1987), analysed serum levels of Copper and Zinc in cases of oral submucous fibrosis and oral cancers. Both were significantly reduced in oral submucous fibrosis. However, Copper/Zinc ratio was found to be elevated in oral

submucous fibrosis. Borle and Jagtap (1987), Estimated complement C'_3 in oral submucous fibrosis and found its level was unaltered.

Some genetic studies have also been undertaken to throw light on the genetic susceptibility in this disease. Cannif et al. (1985), taking into consideration that all autoimmune disease shows disturbance in the frequencies of HLA antigen, performed HLA typing of the patients of oral submucous fibrosis and controls of the same ethenic origin. They observed raised frequencies of A-10 and D-R3. Their findings supported the concept that oral submucous fibrosis is a chronic autoimmune disease, initiated by constituents of betel nut and occurring in genetically susceptible individuals. Genes situated in the HLA region are important determinants of genetic susceptibility in oral submucous fibrosis.

These immunological observations suggest that oral submucous fibrosis fulfil the criteria of autoimmunity. Laid down by Mackey and Burnet (1963).

Pathological Study Of Oral Submucous Fibrosis:

The majority of studies Sharan (1959), Rao (1962), Sirsat and Khanolkar (1957 and 1962) and Wahi (1966) have described the histological changes of the subepithelial tissue in oral submucous fibrosis. Sharan (1959) described hypertrophy with occasional areas of atrophy, Rao (1962) described tobacco tar paintings on the skin to induce progressive epithelial hyperplasia followed by areas of cellular atypism.

Sir sat and Khanolkar (1957 and 1962) described a thickened epithelium with deep invaination into subjascent lamina propria.

Epithelial Changes:

An evaluation of epithelial changes in the different grades of Oral Submucous Fibrosis shows that increase in the clinical severity of the disease may be accompained by epithelial hyperplasia or atrophy, which is associated with an increased tendency for keratinizing metaplasia (Bulletin of WHO 1994).

Wahi et al (1966) correlated the type of keratinizing metaplasia with the site of lesion and the habits of the patients. Lesions involving the palate showed predominantly orthokeratosis and those of the buccal mucosa, parakeratosis. The high mitosis count in parakeratotic epithelia, which is more common with Oral Submucous Fibrosis and the association with parakeratotic leukoplakia predisposes to carcinoma.

Sub Epithelial Changes:

In oral submucous fibrosis the Juxta epithelial tissue shows dense hyalinization and fibrosis. Some may have other different combination of type of juxta epithelial tissue. i.e., dense and fibrillar, loose and fibrillar, and loose and hyalinized. In Majority, the blood vessels in juxta epidermal connective tissue are constricted, but in some instances they may be dilated; Constriction of blood vessels is more in tobacco users than in non tobacco users.

The more advanced lesions had an increased frequency and severity of epithelial hyperplasia and atypism. Hyperchromatism, variation in nuclear/cytoplasmic ratio, spindling of nuclei and down ward projection of basal cells are the prominent features of submucous fibrosis. Connective tissue changes in submucous fibrosis have been variably interpreted, Sirsat, and Khanolkar (1957 and 1962) Sharan (1959) and Rao (1962) have described marked increase in dense collagen in subepithelial tissue. Sirsat and Khanolkar (1962) and Sharan (1959) have also described hyalization of connective tissue. The changes in connective tissue have been interpreted as fibronoid degeneration by Sharan (1959) and elastic degeneration by Sirsat and Khanolkar (1962) Rao (1962) on the other hand did not find elastic or fibronoid degeneration. It is suggested that the connective tissue changes may proceed any epithelial anomaly or may be concomitant. The epithelial and connective tissue changes seem to depend on the effect of tobacco on tissues preconditioned by vitamin deficiencies (Wahi, et al. 1966). However, the epithelial changes may be aggravated by the abnormalities of underlying connective tissue and blood vessels, which may act interfering with metabolic exchange or by the direct effect of the products of degeneration of altered metabolism. The products of degeneration have been considered to have growth promoting properties (Varoni, 1951) and thus the epithelial changes may be secondary to the connective tissue changes.

Histology According to Stage:

On the basis of the histopathological appearances of stained sections, the surgical specimens from Oral Submucous Fibrosis can be grouped into four clearly definable stages (Sirsat SM, Pindborg JJ, 1967) i.e., very early, early, moderately advanced and advanced. These stages are based not only on the amount and nature of the subepithetlial collagen but also on the following criteria –

(a) Presence or absence of oedema

(b) Physical state of mucosal collagen

(c) Overall fibroblastic response (number of cells and age of individual cells)

(d) State of blood vessels

(e) Predominant cell type in the informatory exudate.

Very Early Stage: -

It is characterized by finely fibrillar collagen dispersed with marked oedema. The fibroblastic response is strong with plump young cells containing abundant cytoplasm. The blood vessels are sometimes normal, but more often they are dilated and congested. Inflammatory cells, mainly polymorphoneuclear leucocytes with an occasional eosinophil are present.

Early State: -

The Juxta epithelial area shows early hyalinization. The collagen is still seen as separate bundles, which are thickened. Plumps young fibroblasts are present in

moderate numbers. The blood vessels are often dilated and congested. The inflammatory cells are mostly mononuclear lymphocytes, eosinophils and an occasional plasma cell.

Moderately Advanced Stage:-

The collagen is moderately hyalinized, the amorphous change starting from the juxta epithelial basement membrane. Occasionally thickened collagen bundles are still seen separated by slightly residual oedma. The fibroblastic response is less marked, the cells present being mostly fibrocytes with elongated spindle shaped nuclei and scanty cytoplasm. Blood vessels are either normal or constricted as a result of increased surrounding fibrous tissue. The inflammatory exudate consists of lymphocytes and plasma cells although an occasional eosinophil is also seen.

Advanced State :

The collagen is completely hyalinized and is seen as a smooth sheet, with no separate bundles descernable. Oedema is absent. The hyalinized areas are devoid of firoblasts, although a thin elongated cell or a vestigial nucleus is seen at same interval along the fibre bundle. Blood vessels are completely obliterated or narrowed. The inflammatory cells are lymphocytes and plasma cells.

Oral submucous Fibrosis: A Precancerous Condition

The possible precancerous nature of oral submucous fibrosis was first reported by Paymaster in 1956. While working on oral submucous fibrosis in Bombay he

described development of slow growing squamous cell carcinoma in one third of the cases of this disease. But Sirsat and Khanolkar (1962) could not support Paymaster's findings. Pindborg et al. (1965) demonstrated leukoplakia of oral cavity in 26.9% patients of oral submucous fibrosis. Their findings were based on observations made on 101 patients of oral submucous fibrosis in Northern India. Where as, they reported, the incidence of oral leukoplakia without oral submucous fibrosis was only 3% (19,899 patients were observe). Zacharia and associates (1964) found frequency of oral cancer as 1.2% in patients of oral submucous fibrosis. In Cancer Institute, Trivandrum, they found that the oral cancers share was 36.6% of all reported cancer (1963 observation) and most of the oral cancers patients were having the clinical findings of oral submucous fibrosis.

In order to clearify a possible relationship between oral cancer and oral submucous fibrosis, Pindborg and Zacharia (1965) examined 100 patients with oral cancer and found that 40 of them were having clinical signs and symptoms of oral submucous fibrosis. In their report Pindborg et al. (1965) found leukoplakia, which is an established precancerous condition in 46.7% cases of oral submucous fibrosis. He observed several cases of oral cancer and oral submucous fibrosis occurring together not only in India but In Sri Lanka, Malaysia, Nepal, Thailand and South Vietnam also. They came to conclusion that oral submucous fibrosis was possibly serving as precancerous condition for oral malignancies.

The findings described by Pindborg et al. (1965) lend support to the concept that oral submucous fibrosis is a precancerous condition. In supports of conclusions made by them, they explained the pathogenesis of oral submucous fibrosis based on histopathological observations. In patients of oral submucous fibrosis, the oral epithelium became atrophic and thus more vulnerable to carcinogens which, in India, are not infrequently present in the form of chewing tobacco, spices, chilies, betel leaves and betel nuts. The atrophic epithelium first became hyperkeratotic (Clinically leukoplakia) and later inters cellular oedema and basal cell hyperplasia developed. From these precancerous developments oral carcinoma could develop at any time.

Working, over a period of seventeen years, on malignant transformation rate in oral submucous fibrosis in Kerala, Murti et al. (1985) found that oral cancers were presented in 7.6% cases. The malignant transformation rate in the same sample was 4.5%. Their findings imparted a high degree of malignant potential to this disease. Laskaris et al. (1981) described the potential of disease as a predisposing factor for the development of the malignancies of oral cavity and reported one case of transformation of oral Submucous fibrosis in carcinoma. Mc Gruk and Craig (1984) also demonstrated malignant transformation of oral submucous fibrosis in two Asians immigrants to the United Kingdom. Their observation also, supported high malignant potential to oral submucous fibrosis.

Murti (1985) found co-existence of oral cancer in 10% cases of oral submucous fibrosis. When, co-existence and malignant transformation were considered together, this incidence was 13.5%. He found leukoplakia in 26% cases. Observation of histopathological reports of all oral submucous fibrosis patients brought the picture squamous cell carcinoma in 12%, epithelial dysplasia in 26% and atrophic epithelium in 76% cases.

Rajendran et al. (1986) assessed cell-mediated immunity and humoral response in oral submucous fibrosis and oral cancer and found similar pattern of changes in both conditions. They indicated that oral submucous fibrosis could be an intermediary stage in the malignant transformation of normal cells. These findings reinforced the hypothesis that oral submucous fibrosis is a precancerous condition.

Differential Diagnosis :

In the differential diagnosis Scleroderma must be excluded. Other conditions from which oral submucous fibrosis must be distinguished include leprosy, Hyalinosis cutaneous mucose, Intra oral scarring from epidermolysis bullosae and an extension of the pharyngeal lesion sometimes seen in case of iron deficiency anemia. Oral submucous fibrosis bears a resemblance to localized Scleroderma, which is also a disease of unknown etiology affecting the connective tissue. In each of these two diseases females are affected more often than males. The age range is 70 to 50 years, in duration and hyperpigmentation are clinical features, chest radiographs are normal,

the red blood cell count also decreases. Hyalinized material is deposited in the connective tissue, and abnormal light staining collagen fibres are characteristic. Both disease give response to steroids and hylase therapy. The salient difference between the two conditions is that oral submucous fibrosis is localized to oral mucosa and pharynx and does not affect cutaneous structures, where as scleroderma lesions can occur throughout the body.

Other white lesions of oral mucosa are Leukoplakia, Leukoderma, Lichen planus and oral cancer, Pindborg (1968). Which can be distinguished easily even on clinical examination. In this survey in Bangalore, Lucknow, Bombay the commonest lesion of oral cavity was Leukoplakia, and other lesions were Leukoderma submucous fibrosis, lichen planus and oral cancer.

Table 8 – Frequency of various oral mucosal lesions in different cities of India.

Clinical Diagnosis	Bangalore	Lucknow	Bombay
Oral Cancer	37	24	11
Leukoplakia	155	328	284
Leukoderma	164	166	96
Submucous fibrosis	18	51	50
Lichen planus	2	19	22

Treatment:

In early days, the treatment was purely imperical and consisted of injections of vitamin A & E, Gold injections, injection of fibrinolysin and Iodine.

Joshi (1953) tried Arsenotyphoid injections without any significant regression of the disease. However, cortisone therapy achieved remarkable success (Rao, 1954). De Sa (1954) too noted a similar experience with corticosteroid administrated by parental or oral routes. However, they noted better response only in early stage of the disease (Stage I & stage II).

Schwartz (1952) also found cortisone produce alleviation of symptoms in one case treated by him in Kenya. De Sa (1957) observed 64 cases and found that on two years follow up after treatment, there was a gradual recurrence of symptoms in majority of the patients. He treated cases with systemic administration of hydrocortisone.

Sirsat and Khanolkar (1962) came to conclusion that cortisone affords temporary relief from the disabling symptoms in the early stage of this long standing disease. Rao (1961) concluded that cortisone and its other purified derivatives (Hydrocortisone, Deltacortisone Triaminolone, Dexamethasone) in the form of tablets, systemic injections and local injections were of great help. Rao (1961) advocated definite course of treatment which consisted of 7 weeks treatment with Triamcinolone or Dexamethasone in gradually decreasing dose, starting with 600 mg Triamcinolone

or 90 mg Dexamethasone. This was supplemented with hydrocortisone local injections of 25 mg per time biweekly into the affected area (usually 15 to 20 injections). Since the hydrocortisone was fibrinolytic, antiallergic and anti-inflammatory reduced the oedema. With the above course of treatment Rao (1961) found remarkable improvement in the disease.

In early days of treatment with corticosteroids, Rao (1961) found glycosuria, moon face and generalized oedema. But as the treatment advanced with latest derivatives of corticosteroids, these unwanted symptoms were negligible. He advocated three injections of ACTH (20 IU) to be given for three successive days before the treatment was concluded.

Moos (1968) strongly advocated eradiction of chronic irritation of any form, either mechanical (sharp jagged tooth) or chemical (betel nut and beta chewing, alcohol, smoking and tobacco chewing), along with the subjective treatment, Since most of the cases, reported from India, were anemia, a balanced diet was essential. He was of the strong opinion of the supplementation of vitamins in the initial phase of treatment. Though the vitamin supplementation therapy had been proved of little value by itself (Sirsat and Khanolkar, 1962), but along with other treatments, the improvement was found to be much better, Moos (1968) also tried hydrocortisone therapy and surgical cutting of fibrous band but came to conclusion that these two management gave good result initially but the long term result of such management

still remained doubtful. Fibrous contracture might resulted at the operated site resulting more severe symptoms.

Sinha (1978) tried intra oral injections of hydrocortisone and placental extracts (Placentrax) and paid attention to the improvement of disease. He found improvement in both of the regimes but it was far superior with cortisone as compared to placental extracts. The improvement in Symptomatology, like improvement in suppleness of oral tissue, regaining of pink coloured buccal mucosa, burning sensation, improvement in protusion of tongue as well as in inability to open mouth and reduction in fibrous bands of oral cavity were found to be better in hydrocortisone therapy.

Beside the improvement with hydrocortisone treatment, Sinha (1978) observed that failure rate was four times higher with placental extract. When the failure cases of placentrax were switched over to hydrocortisone therapy the result was quite good while the hydrocortisone failure case could not got improvement with placental extract.

Two years later Sinha (1980) conducted another therapeutic study. He compared the treatment with intra oral injection of hyaluronidase (hylase) and hydrocortisone, and combination of these two drugs in the treatment of oral submucous fibrosis. He found that there was better response in patient treated with hydrocortisone as compared to hylase. The failure rate was less with hydrocortisone

treatment. When the treatment of failure cases were exchanged, they found that the success rate in hylase failure case (i.e. treated with hydrocortisone) was far better than hydrocortisone failure cases (i.e. treated with hylase). Above all, Sinha (1980) obtained best result with combination of hylase and hydrocortisone therapy.

Kakar et al. (1986) tried four regimens and compared the improvement. These regimens were local dexamethasone, local combination of hyaluronidase and dexamethasone and local placental extract. They found that there was quicker response with hyaluronidase but long term and better response was obtained with combination of dexamethasone and hyaluronidase. They recommended this regimen for the management of oral submucous fibrosis.

Considering it as a collagen disorder some workers tried collagenase for the management of oral submucous fibrosis. Chen and Lin (1986) used intra oral injections of collagenase in the treatment of the disease. They found remarkable success in the improvement, but the remission was not complete.

Sharma et al. (1987) searched a new dimension of treatment, giving emphasis to the incomplete remission of by treatment. They advocated vasodilators for the management of oral submucous fibrosis. Nylidrin hydrochloride, a peripheral vasodilator, was experienced for over 10 years. There was reportedly no side effect except complaints of flushingly warm skin. Supportive therapy of vitamin A, E & B,

complex, iodine and placental extract were given. They found success rate of 62.07% in cases of oral submucous fibrosis.

Surgical Treatment:

Moos (1968) advised surgical cutting of fibrous bands of oral submucous fibrosis. The patients improved immediately from severe trismus. But long standing results were not so good because symptoms reappeared due to scarring at the operated site. Kavarana et al. (1984) tried nasolabial flaps in oral submucous fibrosis to improve trismus. They used bilateral full thickness nasolabial flaps and set it into the defects created by incision in oral mucosa. They compared postoperative rehabilitation with other methods and advocated this technique for all cases of oral submucous fibrosis requiring correction of severe trismus.

The malignant transformations of oral submucous fibrosis were treated according to site and size of the growth and histopathological reports. Almost all workers suggested excision of the growth followed by chemotherapy or radiotherapy depending upon the requirements.

Most of the workers like Sirsat & Khanolkar (1962) and Pindborg et al. (1968) suggested regular follow up of the patients of oral submucous fibrosis, keeping high malignant transformation rate of the disease into mind.

MATERIAL & METHODS

Material and Methods

The present study was conducted on 104 patients attending out door of Department of Otolaryngology. M. L. B. Medical College & Hospital Jhansi, Bundelkhand region (U. P.). During the period of November 1998 to October 2000. Laboratory studies were done by various units of Department of Pathology. The special investigative process like blood biochemistry were done at Vardhman Medical Center, Jhansi. An effort was made to put light on etiology and pathological process of the disease.

Clinical Study:

Selection of patients was based upon the recognized sign and symptom of oral submucous fibrosis. Though the number of reported cases were such more but only those cases had been considered who were being followed up regularly with complete investigative process.

The patients under study, were subjected to thorough investigations. Detailed history was taken and physical examination with complete ENT Check up was done. The patients were kept on regular follow up and the improvement was assessed. Patients were divided into two groups:

1- Control group.

2- *Study group.*

Control Group :

These were those patients of oral submucous fibrosis, who were treated conservatively by mouth wash, analgesic, antioxidants and injection Hydrocortisone locally.

Study Group :

These patients were those who were treated by oral calcium and iron supplementation with mouth wash and analgesic.

Clinical History :

Special attention was done on following points while taking history of the patients –

- *Duration of onset of problem.*
- *Complaints made by patient with chronological order i. e. inability to open mouth, intolerance to hot, spicy food and chillies. Difficulty to protrude tongue, pain and swelling at jaw joint and neck.*
- *Other associated complaints with main complaints like pain in the ears, recurrent stomatitis, nasal voice, nasal regurgitation, repeated ulceration of oral cavity, lose/decrease in taste sensation and inability to blow candle or to whistle were also interrogated.*
- *History of similar episodes in the past and if it was significant, what treatment, patient had taken, with assessment of result.*

Personal History :

Since the personal history is much more significant, special attention was made to bring light on food habit i.e. patient being vegetarian, non-vegetarian or occasionally non-vegetarian, habit of using spices and chillies and the quantity & duration from which these substances being used. Use of any other similar irritating material associated with food habits.

Attention was paid during recording of the personal history of habituation and addictions. Chewing of tobacco with/without slaked lime was considered. Smoking habit and its pattern was also recorded. Use of betel nuts and betel chewing, with or without tobacco, was other area of special consideration. Use of pan masala and other similar commercial preparations, alcohol intake were also interrogated.

Hygiene of oral cavity and methods used by patients to clean teeth and oral cavity were also considered. Questions were asked about use of commercial tooth brushes, tooth paste/powders, use of plant sticks (like Neem or others), ash, charcoal and misi. Attention was paid on use of tooth powders mixed with tobacco (Gul). Questions were asked about how frequent these substances were used.

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Social History:

Social status of the patients was also evaluated with related background of habitat (i.e. rural or urban). Classification of social status was made according to the classification suggested by Central Statistical Organization. Government of India (1962).

1.	Upper Class	-	Principals, Academicians, Doctors, Lawyers, Engineers, Military Officer. Senior Executives & business proprietors.
2.	Upper Middle Class	-	Junior executives, higher secondary school teachers, small business men.
3.	Lower Middle Class	–	Clerks, primary school teachers, skilled labours like mechanics, electrician and formers.
4.	Lower Class	–	Unskilled labours, peon, sweeper porters, shoemakers etc.

History of Previous Treatment :

Patients were asked about their previous treatment history, specific treatment if taken and improvement if obtained.

Other Associated Systemic Disease :

Detailed history was taken about other systemic disorders if present, Attention was paid about tuberculosis, diabetic, rheumatoid disorder, syphilis and lymphadenopathy.

Examination :

After completing detailed history, general and local examinations were performed. General examinations was including general condition of patients i.e. general out look and general built and nutritional status of the patient. Patients were also examined for the occurrence of systemic disease like tuberculosis, diabetes lymphadenopathies, rheumatoid disorders and syphilis.

Local Examination:

Presence of any congenital anomaly, condition of angle of mouth, colour and condition of lips, general hygenic condition of oral cavity, colour of buccal mucosa, palate, tongue and uvula was noted. Concentration was made on the presence of fibrotic bands and its extension to the lateral wall of cheek, palate, uvula and tongue. Palpation of lateral wall of cheek was done bimanual by putting two fingers from inside and supported by two fingers or thumb of other hand from outside, to assess the thickness of fibrotic band. The patients were asked to protrude their tongue to observe ankyloglossia.

Progressive narrowing and inability to open mouth were assessed. It was done by measuring the distance between upper and lower incisors with the help of measuring caliper. The same technique was applied to evaluate the improvement during follow up of the cases and after the treatment. Severity of the trismus was classified into three different groups depending upon distance between upper and lower incisions.

1.	Normal	I - I distance		<	3.5 cm.
2.	Mild	I - I distance	3.1	-	3.5 cm.
3.	Moderate	I - I distance	2.1	-	3.0 cm.
4.	Severe	I - I distance		<	2.0 cm.

Oral cavity was looked also for ulcerated lesions over tongue, cheek, palate, uvula, and lips. Status of teeth and gums were assessed for pyorrhea, cavities, sharp tooth and other associated lesions. Distribution of taste papillae and baldness of tongue were also noted. Ears were examined to rule out any possible disorder in relation to earache. Throat and none were also locked for any possibility of disease.

Observation of leukoplakia and its distributive pattern got a special consideration. Leukoplakic patches over palate, cheek, uvula, tongue and lips were thoroughly examined. Presence of growth weather benign or malignant in any part of the oral cavity were examined and recorded accordingly.

Clinical Stage of Disease :

Clinical staging of the disease was based on its clinical presentation and severity of the symptoms. Present staging of the disease was classified by De'Sa (1957).

Stage	Characteristic
Stage I Early Stage	Burning sensation and irritation with hot spicy food, no clear-cut Fibrotic bands present, Oral Mucosa is blanched and loses its elasticity, No trismus, Slight restriction of mouth opening & tongue protrusion normal.
Stage II Established Stage	Burning sensation and irritation with hot spicy food, Fibrotic bands Present, blanched opaque leather like mucosa, considerable restriction to mouth opening, slight restricted tongue protrusion, Oral hygiene poor.
Stage III Advanced	Burning sensation and irritation with hot spicy food, thick Fibrotic bands Present, blanched opaque leather like mucosa, very little mouth opening, restricted tongue protrusion, Oral hygiene very poor. Speech and eating very much impaired.

Clinical Chemistry Analyzer

Investigations:

Blood samples were collected for haematological, serological and biochemical investigations. Under hematological setup – total leukocytes count, differential leukocytes count and haemoglobin were evaluated. To evaluate haemoglobin, cyanomethhaemoglobin method was employed. Under serological investigations – Erythrocyte Sedimentation Rate (ESR), demonstration of L. E. Cells, ASO and its titre were looked for. In biochemical observations total serum protein, Albumin/globulin ratio and VDRL test were performed. Total Serum calcium and serum iron were done as below mentioned method.

SERUM CALCIUM ESTIMATION :

Principle :

Colorimetric measurement with ortho-cresolphtalein complexion. The 8-hydroxyquinoline prevents mg 2+ from interference upto 4 mmol/L (100mg/L).

Reagents Composition :

Reagent 1 :

Dimethylamine	360	mmol/L

Reagent 2 :

O-cresolphatlein complexion	0.15	mmol/L
8-Hydroxyquinoline	17.2	mmol/L

Standard :

Calcium	10	mg/dL
	100	mg/L
	2.5	mmol/L

Preparation and Satability of Working Reagent

Mix 1 volume of reagent 1 with 1 volume of reagent 2.

Stability : 20 hours at $2 - 8^{0}$ c

Reference Values

	Minimum	Maximum	Unit
Serum, Plasma	8.8	10.2	Mg/dL
	88	102	Mg/L
	2.2	2.55	Mmol/L

Procedure

1 ml of reagent is taken in 3 clean & dry test tubes. 10µL of distilled water is put in blank, 10µL Standard is put into standard test tube and then 10µL sample (Serum) is put into sample test tube. Mix well, and read the optical density (OD) after a 5 minute incubation. The final colour is stable for at least 1 hour.

Wavelength : 570 nm

Temperature : 37^{0}c

Cuvette : 1 cm light path.

Read against reagent blank.

	BLANK	STANDARD	SAMPLE
Reagent	1mL	1 mL	1mL
Dist, Water	10µL	-	-
Standard	-	10µL	-
Sample	-	-	10µL

Mix and read optical density (OD) after a 5 minute incubation. The final colour is stable for at least 1 hour.

Calculation :

OD Sample mg/dL n = 10

----------x n mg/L n = 100

OD Standard mmol/L n = 2.5

n = standard concentration.

Linearity

UP TO 13.5 mg/dL (135 mg/L) (3.40 mmol/L).

SERUM IRON ESTIMATION :

Principle

Serum iron reacts with chromazurol B and cetytrimethyl ammonium bromide to form a coloured complex.

The intensity of the colour is proportional to the iron concentration.

Reagents Composition

Chromazurol B 0.2 mmol/L

Cetyltrimethyl ammonium bromide	2	mmol/L
Guanidine hydrochloride	3	mol/L
Acetate buffer, pH 5.0	45	mmol/L
Standard :		
Iron	100	µg/dL
	1	mg/L
	17.9	µmol/L

Preparation and stability of working reagent

When stored at 250 C and protected from light, the reagents are stable until the expiry date stated on the label.

The reagent is ready for use.

Reference Value

50	-	168	µg/dL
0.5	-	1.68	mg/L
8.95	-	30	µmol/L

Procedure

1 ml of reagent is taken in 3 clean & dry test tubes. 50µL of distilled water is put in blank, 50µL Standard is put into standard test tube and then 50µL sample (Serum) is put into sample test tube. Mix well, and read the optical density (OD) after a 15 minute incubation. The final colour is stable for at least 1 hour.

Wavelength : 623 nm (620 –640)

Temperature : 37 ^{0}C

Cuvette : 1 cm light path.

Read against reagent blank.

	BLANK	STANDARD	SAMPLE
Reagent	1mL	1 mL	1Ml
Distilled Water	50µL	-	-
Standard	-	50µL	-
Sample	-	-	50µL

Mix well, and read the optical density (OD) after a 15-minute incubation. The final colour is stable for at least 1 hour.

Calculation :

OD Sample µg/dL n = 100

----------x n mg/L n = 1

OD Standard µmol/L n = 17.9

n = standard concentration.

Lincarity

UP TO 500 µg/dL (5 mg/L) (89.5 µmol/L).

Diagnosis:

The diagnosis of the disease was based mainly on the clinical presentation. The detailed history and complaint based physical examination was enough to establish the diagnosis.

TREATMENT

Control Group:

These were those patients of oral submucous fibrosis, who were treated conservatively by mouthwash, analgesic, antioxidants and injection hydrocortisone locally once weekly for 5 weeks.

Study Group:

These patients were those who were treated by oral calcium and iron supplementation with mouth wash and analgesic. Calcium was given by oral route as tab. calcium carbonate 500mg b.i.d. with vitamin D-400 i. u. / day. Iron was also given by oral route as tab. Iron (III) Hydroxide polymaltose complex eq. to Elemental Iron 100mg o.d. Iron & Calcium was given with time difference of more than two hours for better absorption because Iron and Calcium inhibit

Beside the medical treatment, all the patients were advised to stop taking tobacco in any form, stop smoking and to avoid any form of chronic irritation like alcohol, betel chewing, using pan masala, spicy food and chilies. Extraction of sharp tooth was advised, if present. They were also advised to clean the oral cavity properly

with adequate tooth powder/paste and tooth brush. Patients were asked to do antiseptic gargle and mouth wash twice daily after each meal, to improve status of oral hygiene.

First Clinical Assessment:

The patients were examined on each visit to assess the improvement but through local and general examination and improvement was assessed after one month of the treatment. Improvement in the symptoms, previously presented by the patients were taken into consideration. Improvement in the colour of buccal mucosa, palate, cheek tongue and lips were observed along with improvement in the protrusion of tongue. The distance between upper and lower incisors was measured to assess the trismus. Minor symptoms, previously presented by the patients, were also examined the improvement.

Second Clinical Assessment:

Second Clinical assessment was done after completing second month of the treatment. Patients were examined for all of the symptoms, presented before. Emphasis was made on same line of observations on which first clinical assessment was done.

Third Clinical Assessment:

Third and final follows check up was done after finishing the treatment (after 3 months). Patients were examined for all of the clinical findings. Relevant and significant investigations were repeated.

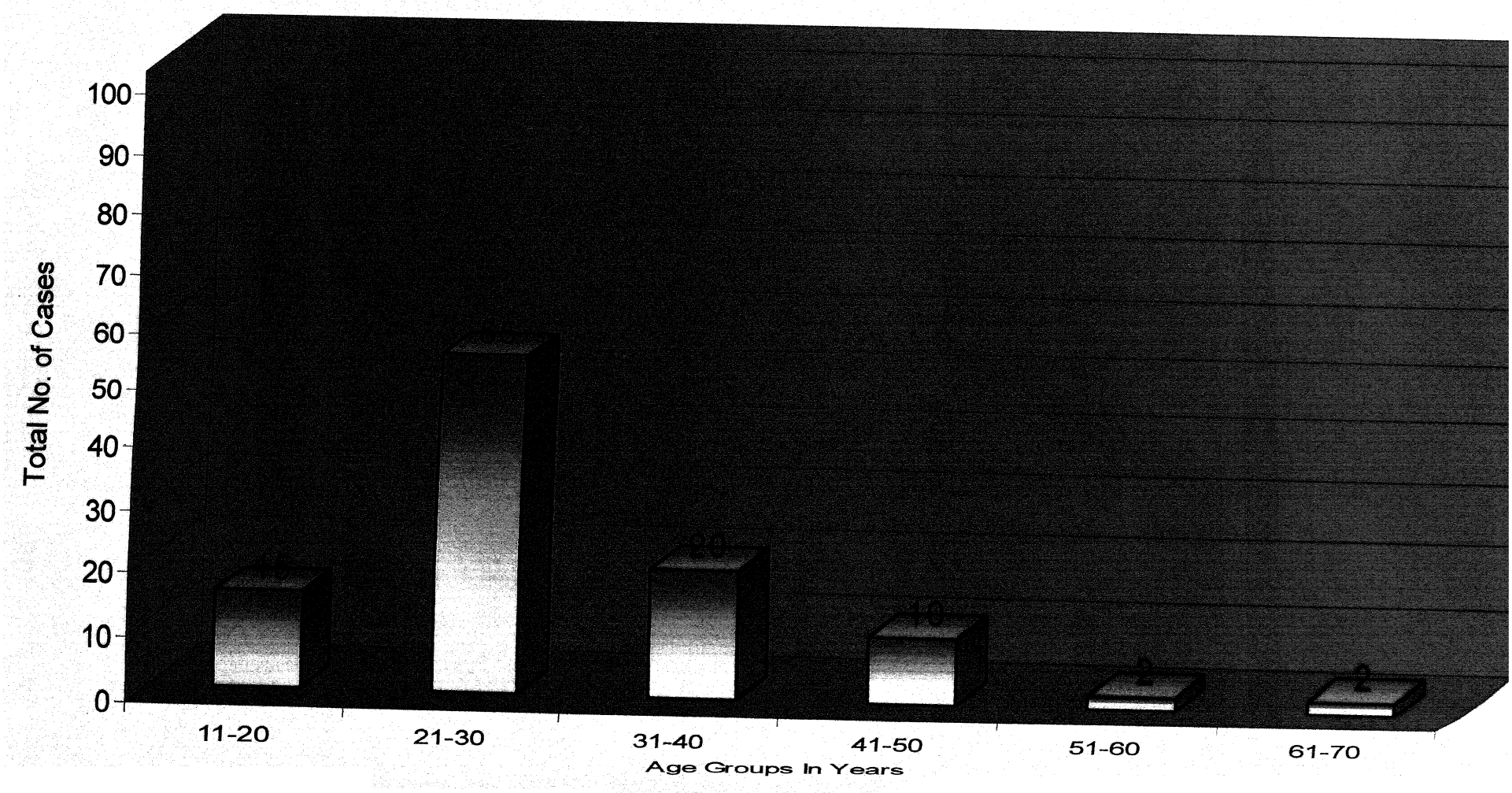
Management of Failure Cases:

Failure cases from each group were subjected to the combination of treatment which was consisting of intra oral hydrocortisone, hyaluronidase, systemic corticosteroid, antioxidants and multivitamin supplementation. The clinical assessments were made according to the previous assessments.

Malignant cases were managed either with surgical excision and radiotherepy or with radiotherapy alone, depending upon the need. Other supportive measures like surgical cutting of fibrous band, or condylectomy if necessary, were performed and the postoperative status of the patients was evaluated.

OBSERVATIONS

Bar Diagram No. 1 Showing The Number of Patients in Various Age groups



Observations

The present study consisted of the observations made on 104 patients who attended the department of Otolaryngology, Institute of M. L. B. Medical College, Hospital, Jhansi between November 98 to October 2000.

The total number of patients of patients of oral submucous fibrosis were more than the cases included into present observation. Some of the reported cases did not turned up after their first or second visit, therefore only cases which were, observed with complete follow up, taken into consideration for the study.

Prevalence :

Table 1 : Showing Prevalence of the Oral Submucous Fibrosis.

Total No. of cases attending ENT OPD during observation (Nov 98 to Oct 2000)	Total No. of Cases of Oral Submucous Fibrosis	Prevalence %
37,440	685	1.81

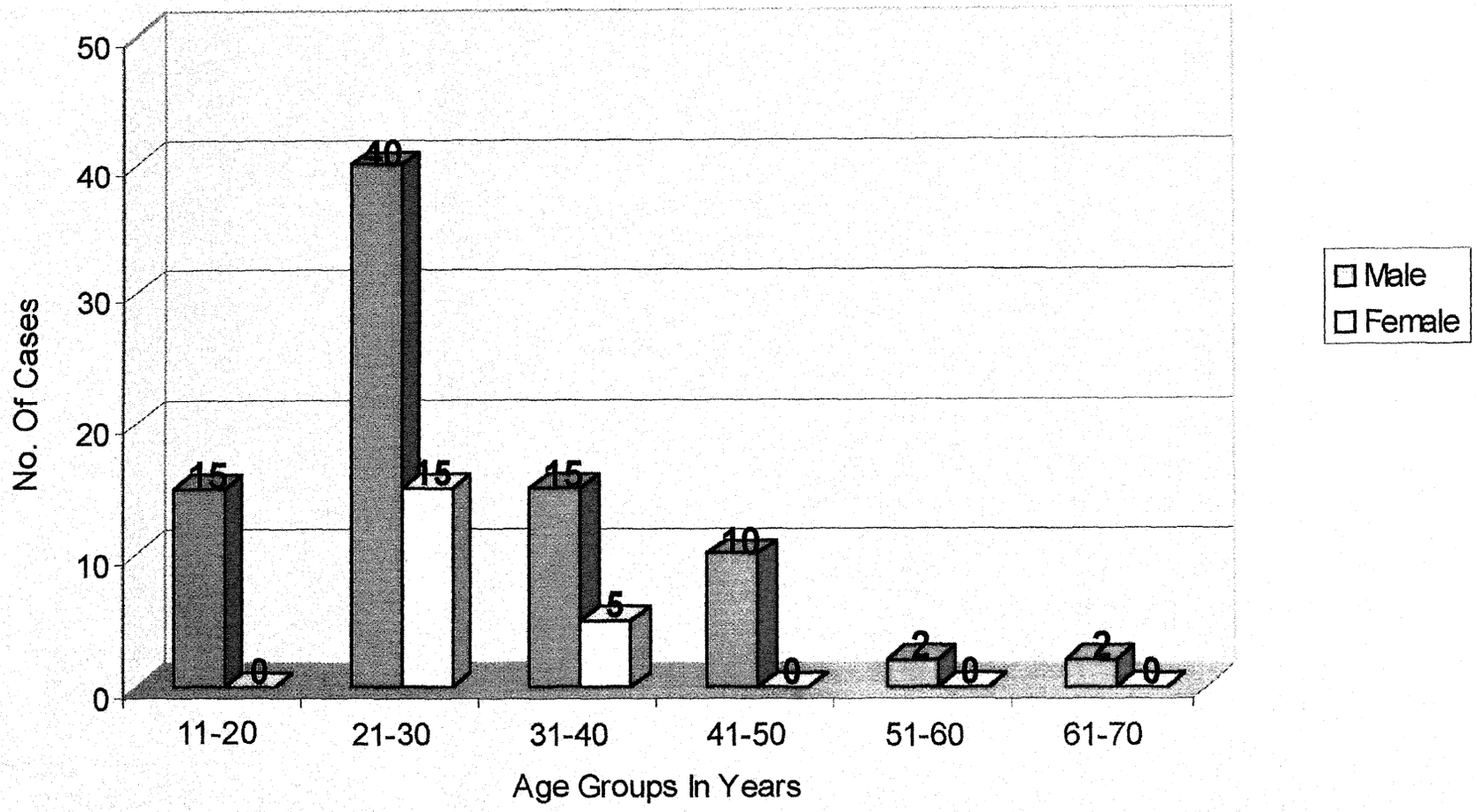
During the period of observations, total number of patients, attending out patient department of E. N. T. were 37,440 number of patients who were diagnosed as oral submucous fibrosis were 685. The prevalence of the disease was found to be 1.81%

Age :

Table No. 2 Showing the Number of Patients in Various Age Group.

Sl. No.	Age Group In Years	Total No. of Cases	Percentage
1.	11-20	15	14.42 %
2.	21-30	55	52.88 %
3.	31-40	20	19.23 %
4.	41-50	10	9.61 %
5.	51-60	2	1.92 %
6.	61-70	2	1.92 %
	Total	104	100 %

Bar Diagram No. 2 Showing Sex Distribution Of The Disease



The incidence of oral submucous fibrosis was maximum in 2nd 3rd & 4th decades of life. These three decades were including 90 patients (86.53%). 14.42% (15) cases were reported from the age group of 11-20 years. The age of youngest patients was 16 years. 52.88% (55) cases were from the age group of 21-30 years, 19.23% (20) cases from 31-40 years age group, 9.61% (10) cases from age group 41-50 and 1.92% (2) cases were reported from the age group of 51-60 years and 61-70 years both. The age of oldest patients was 65 years. There was no any case reported from the age group of <10 and >70 years in present study.

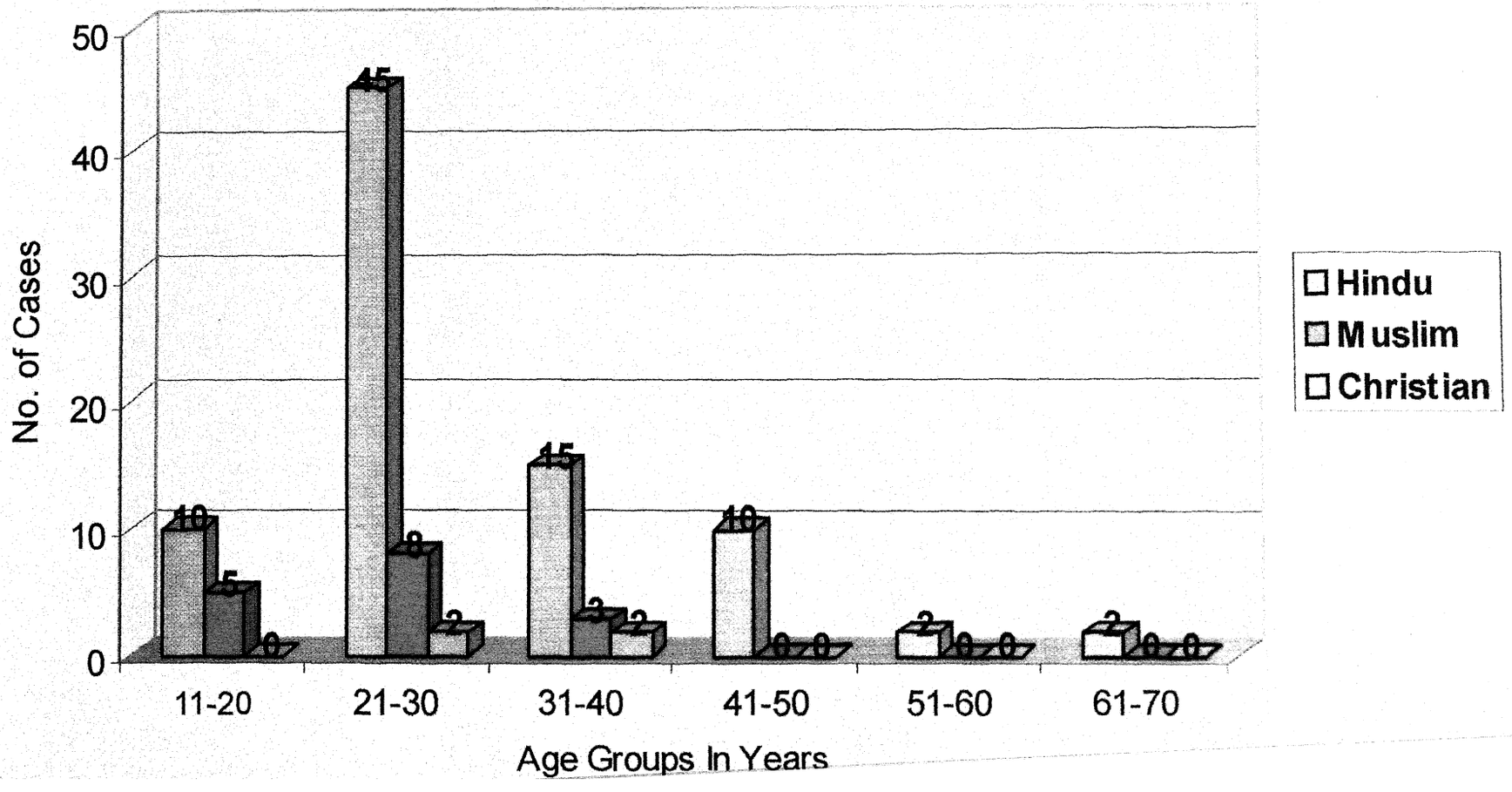
An average age of all reported cases was found to be 26.2 years. The highest incidence of disease 52.88% was observed in third decade of the life. 55 cases were reported from this age group.

Sex:

Table 3 : Showing Sex Distribution of the Disease.

Age Group In Years	Male		Female	
	No.	%	No.	%
11-20	15	14.42%	-	-
21-30	40	38.46%	15	14.42%
31-40	15	14.42%	5	4.60%
41-50	10	9.6%	-	-
51-60	2	1.92%	-	-
61-70	2	1.92%	-	-
Total	84	80.74%	20	19.22%

Bar Diagram No. 3 Showing Incidence of Disease in Various Religions



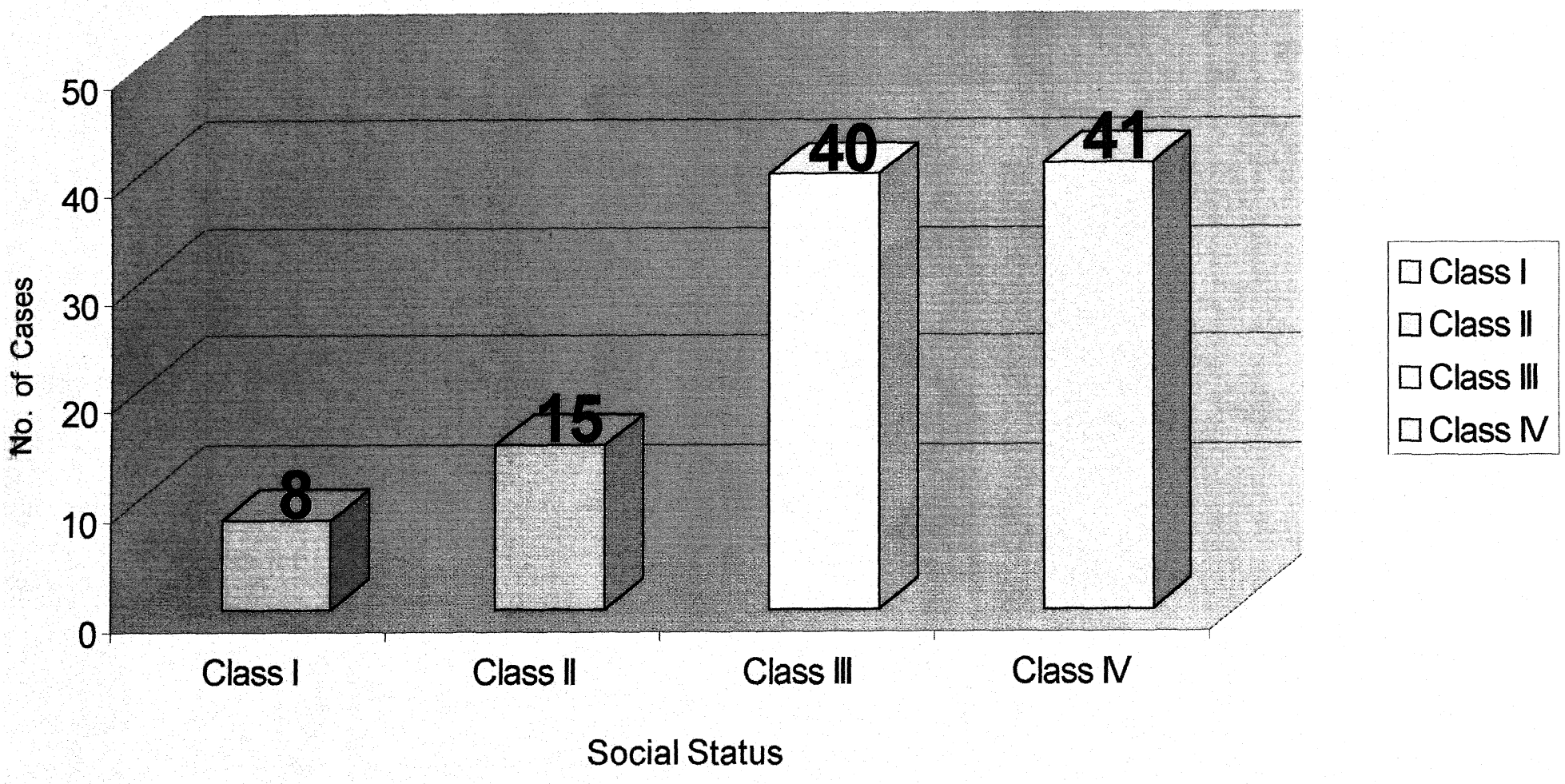
Male and female percentage, out of total cases were 80.74% (84 Cases) and 19.22% (20 Cases) respectively. Not a single female case was reported from age group of 11-20 years and than from 41-70 years. All cases, reported from these age group, were males. The group of 21-30 year was comprised of 38.46% (40 Cases) of males and 14.41% (15 Cases) of females while these percentage were 14.42% (15 cases) male and 4.60% (5 cases) female in age group 31-40 years in the successive age groups, the male percentage were 9.6, 1.92 and 1.92 respectively. Male and female ratio was found to be 4 : 1.

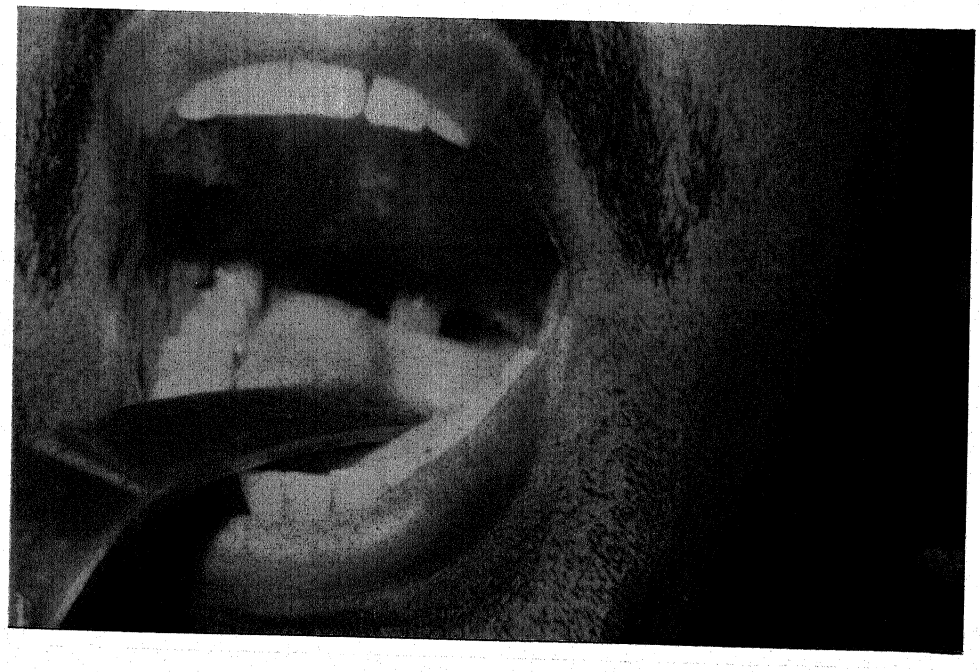
Religion :

Table 4 : Showing incidence of disease in various religions.

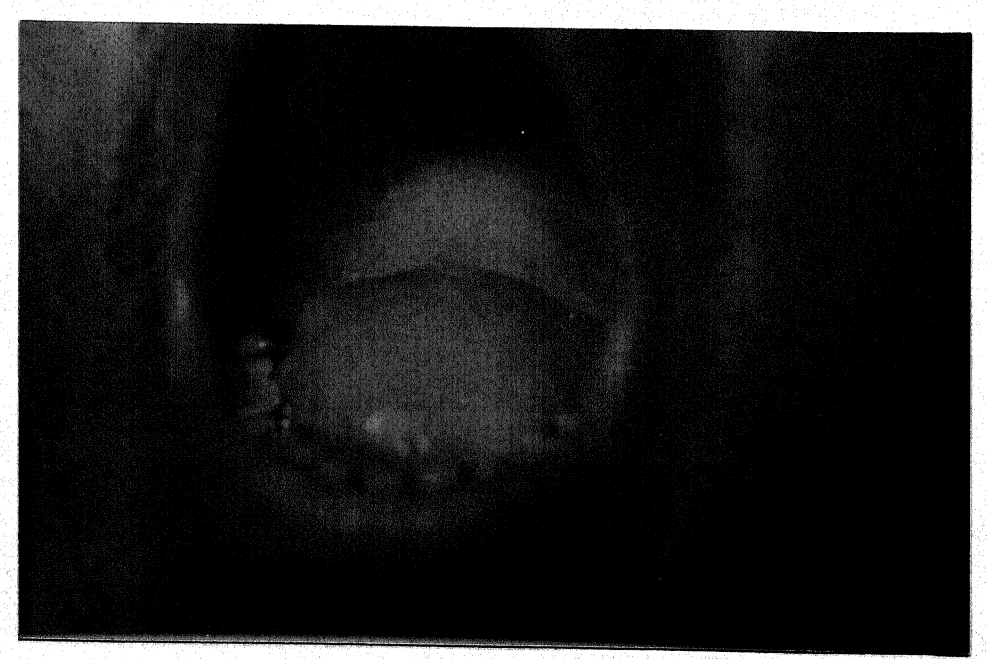
Age Group	Hindu		Muslim		Christian	
In Years	No.	%	No.	%	No.	%
11-20	10	66%	5	33%	-	-
21-30	45	81%	8	14%	2	3.6%
31-40	15	75%	3	15%	2	10%
41-50	10	100%	-	-	-	-
51-60	2	100%	-	-	-	-
61-70	2	100%	-	-	-	-
Total	84	80.76%	16	15.38%	4	3.8%

Bar Diagram No. 5 Showing Social Status of the patients





Leukoplakia right cheek with Oral Submucous Fibrosis



Fibrosis of palate with baldness of tongue

Social Status :

Table : 6 Showing social status of the patients.

Age Group In years	Total No. of patients	Class I		Class II		Class III		Class IV	
		No.	%	No.	%	No.	%	No.	%
11-20	15	-	-	-	-	10	(66%)	5	(33%)
2130	55	5	(9%)	8	(14.5%)	21	(38%)	21	(38%)
31-40	20	3	(15%)	5	(25%)	5	(25%)	7	(35%)
41-50	10	-	-	2	(20%)	2	(20%)	6	(60%)
51-60	2	-	-	-	-	2	(100%)	-	-
61-70	2	-	-	-	-	-	-	2	(100%)
Total	104	8	(7.6%)	15	(14.42%)	40	(38.46%)	41	(39.42%)

Out of Total of 104, 8 cases (7.6%) were from class I Social Status 15 cases (14.42%) from class II and 40 (38.46%) from class III the maximum number from class IV 41 cases (39.42%)

Clinical Presentation :

Table : 7 Showing clinical presentation of various symptoms.

Out of 104 cases, 89 cases (85.5%) had difficulty to open the mouth, 85 cases (81.7%) had intolerance to hot & spicy food, 40 cases (38.46%) had inability to protrude tongue, while only 3 cases (2.8%) showed pain and sewlling in jaw and neck. Nasal Voice was present in 15 cases (14.42%), 3 cases (2.8%) had nasal regurgitation, 12

Bar Diagram No. 6 Showing Clinical Presentation of the Disease

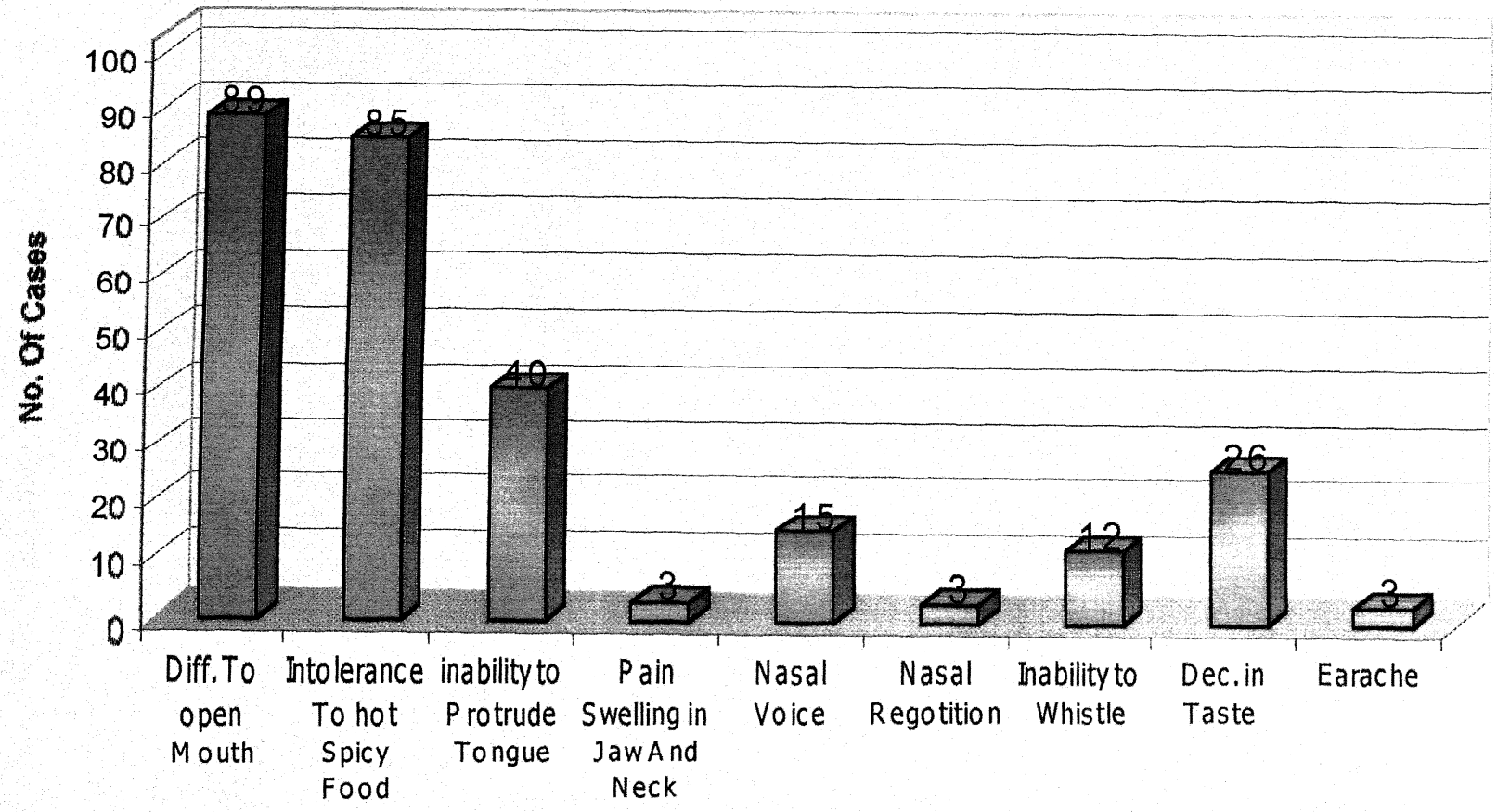
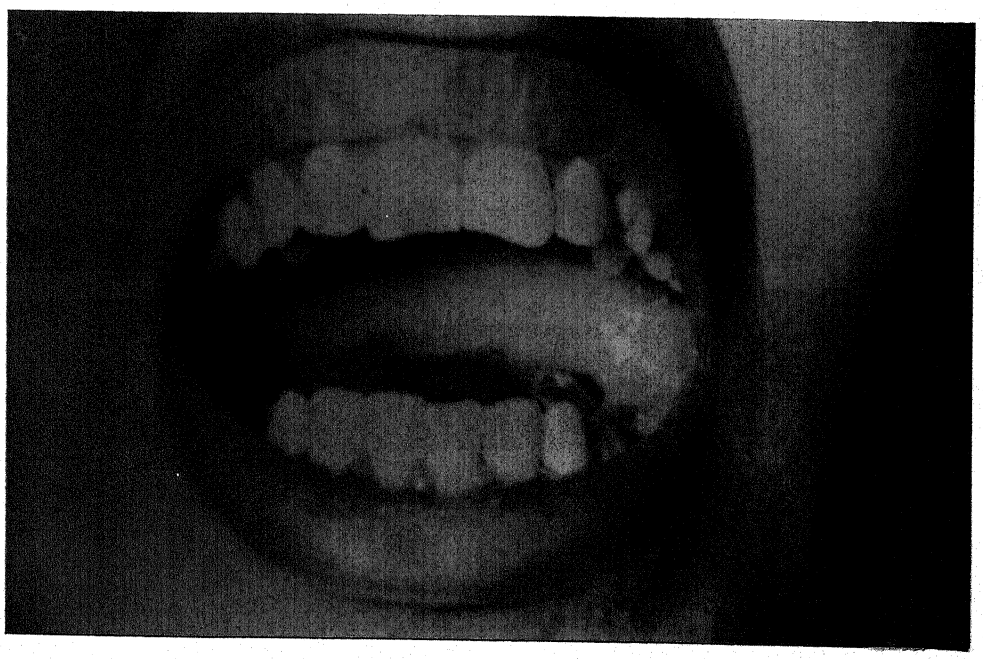
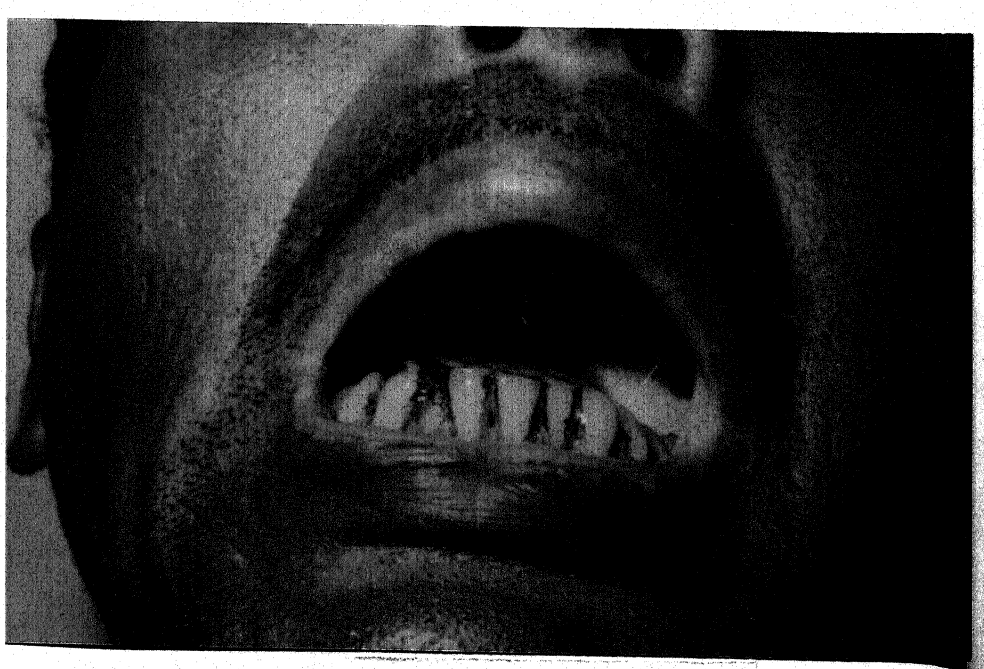


Table : 7 Showing clinical presentation of various symptoms.

Age Group In Years	Total No. of Patients	Difficulty to open mouth		Intolerance to Hot Spicy Food		Inability to Protrude tongue		Pain & Swelling In jaw & neck		Nasal Voice		Nasal Regurgitation		Inability to Whistle		Decrese in Taste sensation		Earache	
		No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%
11-20	15	12	80%	13	86%	3	20%	-	-	3	20%	-	-	3	20%	3	20%	-	-
21-30	55	47	85%	45	81.8%	28	50%	2	3.6%	7	12.7%	2	3.6%	7	12.7%	12	21.8%	3	5.45%
31-40	20	18	90%	16	80%	2	10%	-	-	-	-	-	-	2	10%	5	25%	-	-
41-50	10	8	80%	7	70%	3	30%	1	10%	2	20%	1	10%	-	-	3	30%	-	-
51-60	2	2	100%	2	100%	2	100%	-	-	1	50%	-	-	-	-	1	50%	-	-
61-70	2	2	100%	2	100%	2	100%	-	-	2	100%	-	-	-	-	2	105%	-	-
Total	104	89	85.5%	85	81.7%	40	38.46%	3	2.8%	15	14.42%	3	2.8%	12	11.5%	26	25%	3	2.8%

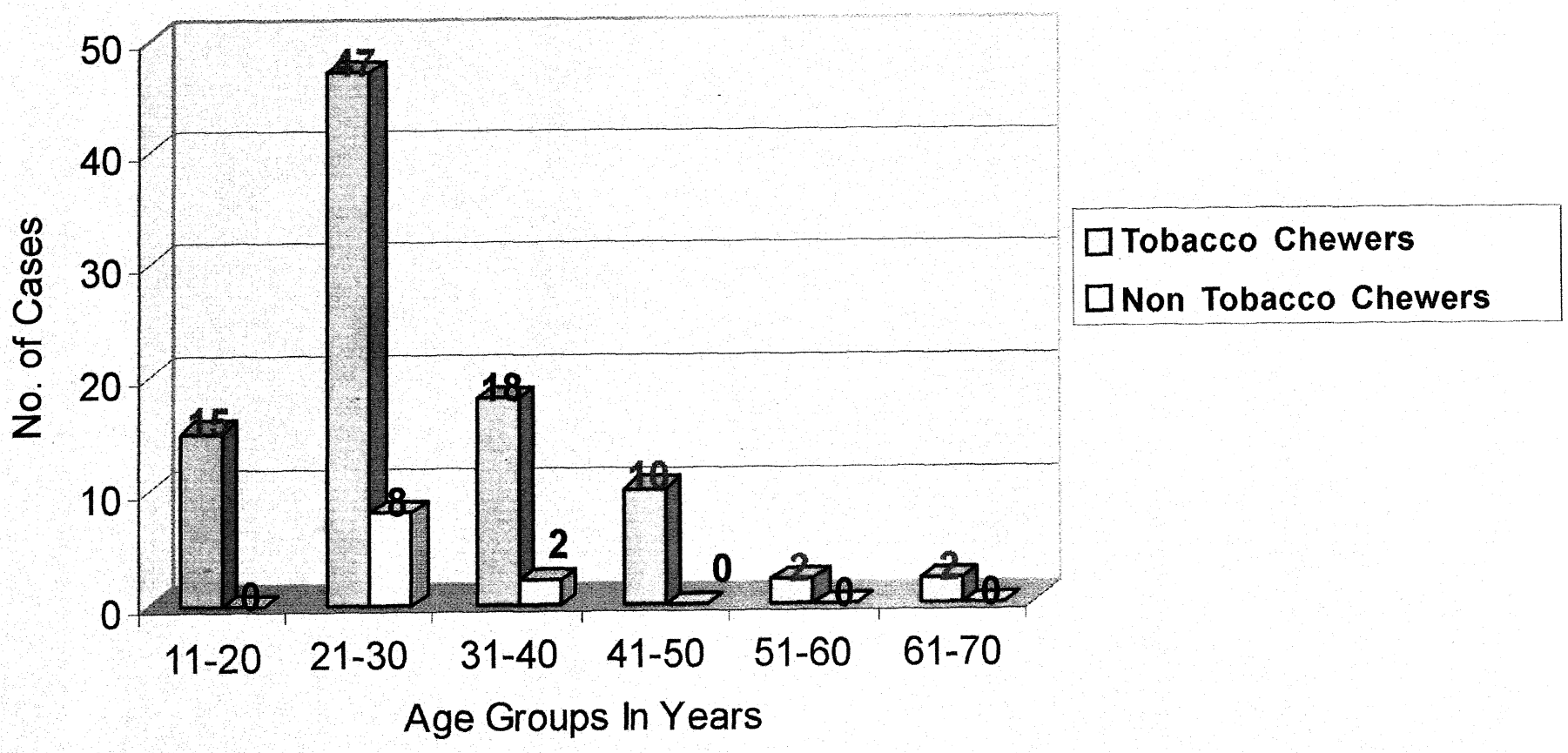


Oral Submucous Fibrosis in a young female



Fibrosis of left cheek

Bar Diagram No. 7 Showing Incidence of Tobacco Chewing in the disease



cases (11.5%) had inability to whistle. Decreases in taste sensation were present in 26 cases (25%) while only 3 cases (2.8%) showed Earache.

Personal Habits : Tobacco Chewing

Table : 8 Showing incidence of tobacco chewing

Age Group In Years	Total No. Cases	Tobacco Chewing		Non Tobacco Chewing	
		No.	%	No.	%
11-20	15	15	100%	-	-
21-30	55	47	85%	8	15%
31-40	20	18	90%	2	10%
41-50	10	10	100%	-	-
51-60	2	2	100%	-	-
61-70	2	2	100%	-	-
Total	104	94	90%	10	9.6%

From 104 reported cases, 94 cases(90%) had habit of tobacco chewing. This habit was recorded only in those cases who were practising this habit not less than one year. 100% of cases 15 from first age group (11-20 years) were found to have this habit. In 2nd age group (21-30 years) 47 cases (85%) were tobacco chewer while 8 cases (15%) were non chewer. In the age group of (31-40 years) 18 cases (90%) were tobacco chewer and 2 cases (10%) were non tobacco chewer. In age group of (41-50 years) (51-60 years) and (61-70 years) all reported cases were tobacco chewers.

Bar Diagram No. 8 Showing Site of Submucous Fibrosis in Oral Cavity

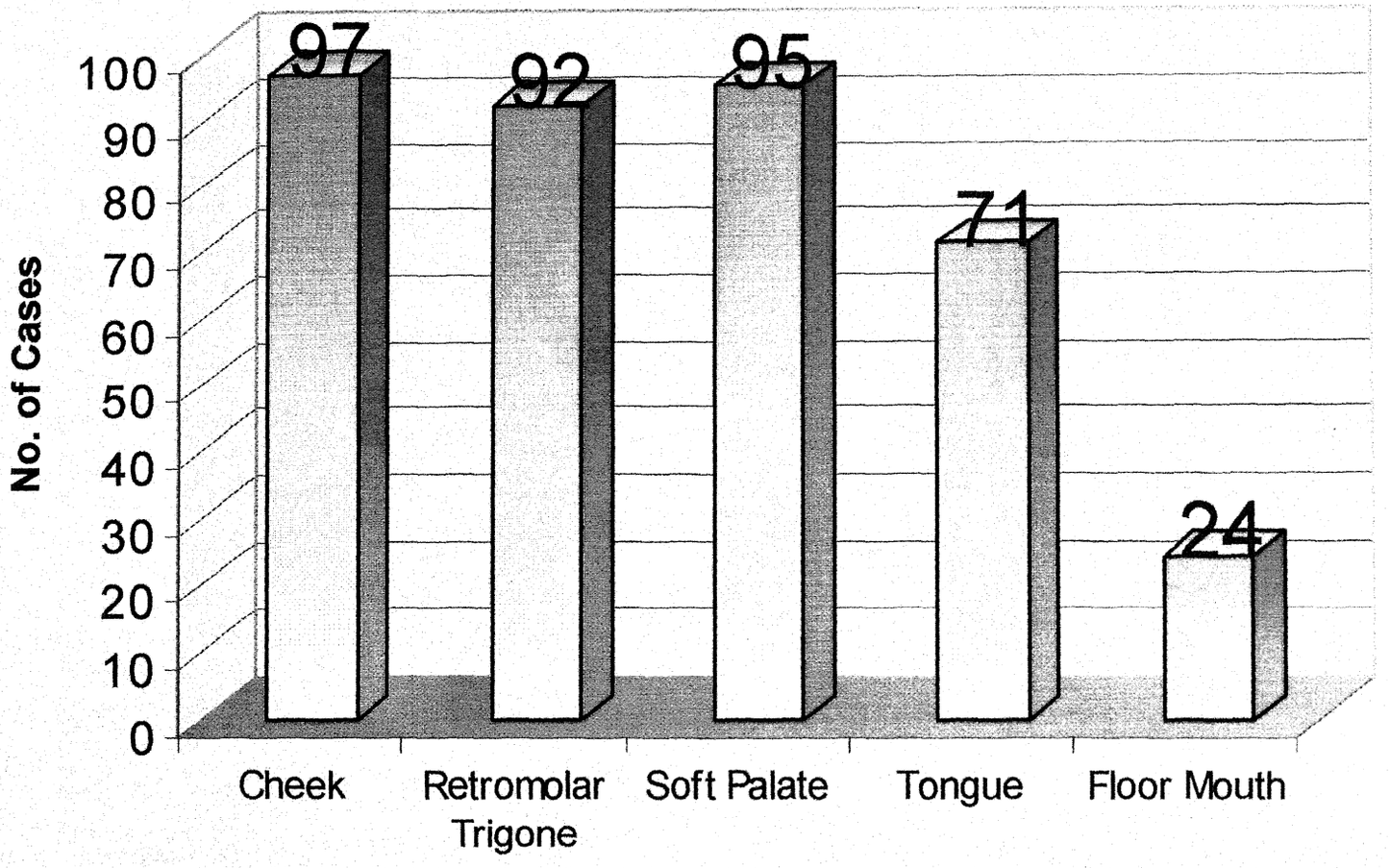


Table 9 : Showing site of Sub Mucous fibrosis in Oral Cavity

Age Group In Years	Total No. of Patients	Cheek		Retromolar Trigone		Soft Palate		Tongue		Floor of Mouth	
		No.	%	No.	%	No.	%	No.	%	No.	%
11-20	15	15	100%	12	80%	13	86%	7	46%	2	13.3%
21-30	55	48	87%	50	90%	52	94%	40	72%	11	20%
31-40	20	20	100%	18	90%	18	90%	14	70%	4	20%
41-50	10	10	100%	8	80%	8	80%	6	60%	3	30%
51-60	2	2	100%	2	100%	2	100%	2	100%	2	100%
61-70	2	2	100%	2	100%	2	100%	2	100%	2	100%
Total	104	97	93%	92	88%	95	91%	71	68%	24	23%

Submucous Fibrosis Involving Tongue

Fibrosis of palate with ulcerative lesions on left side

Bar Diagram No. 9 Showing Clinical Stages of Disease

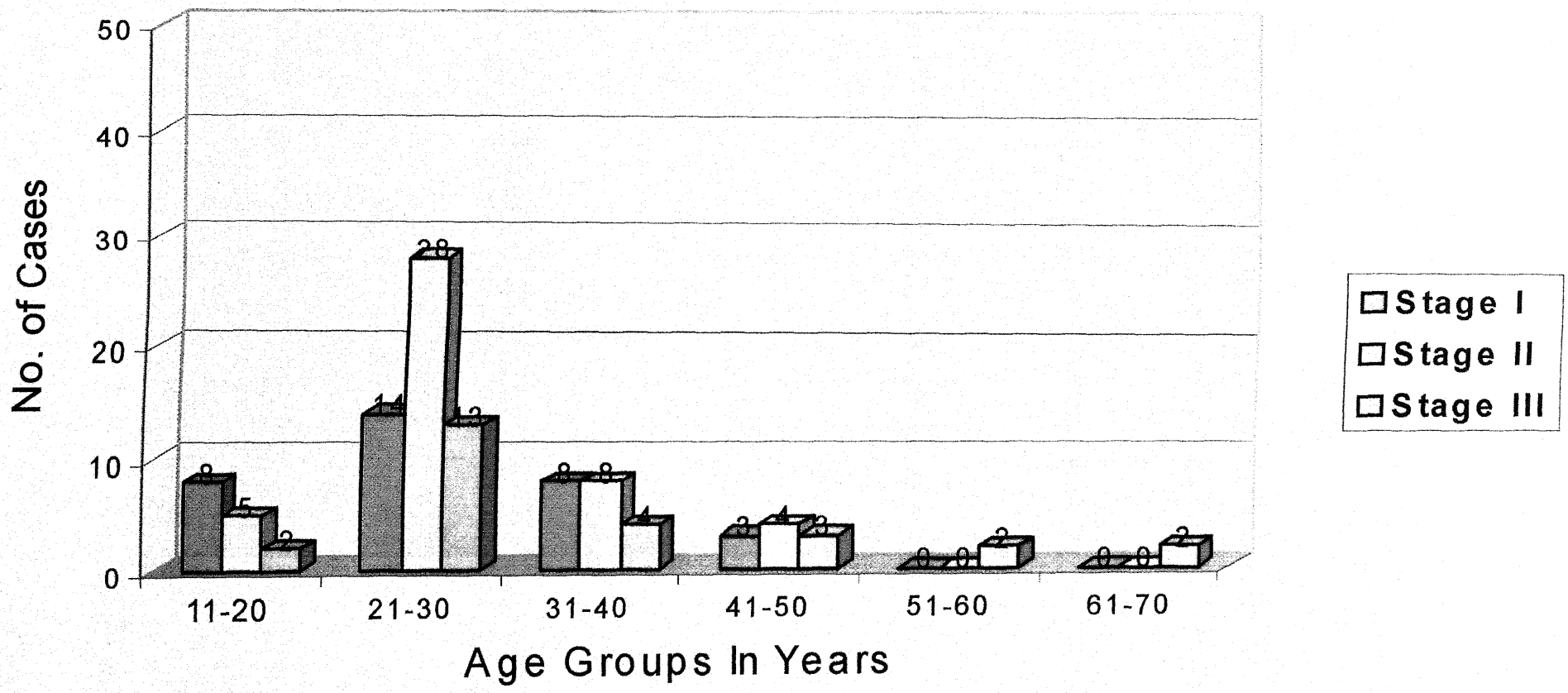


Table 9 : Showing site of Sub Mucous fibrosis in Oral Cavity.

Out of 104 patients 97 cases (93%) had Fibrosis in cheek region, 92 cases (88%) had fibrous bands in Retromolar Trigone, Soft Palate involvement were in 95 cases (91%), tongue involvement were present in 71% cases (68%) while only 24 cases (23%) had involvement of Floor of mouth.

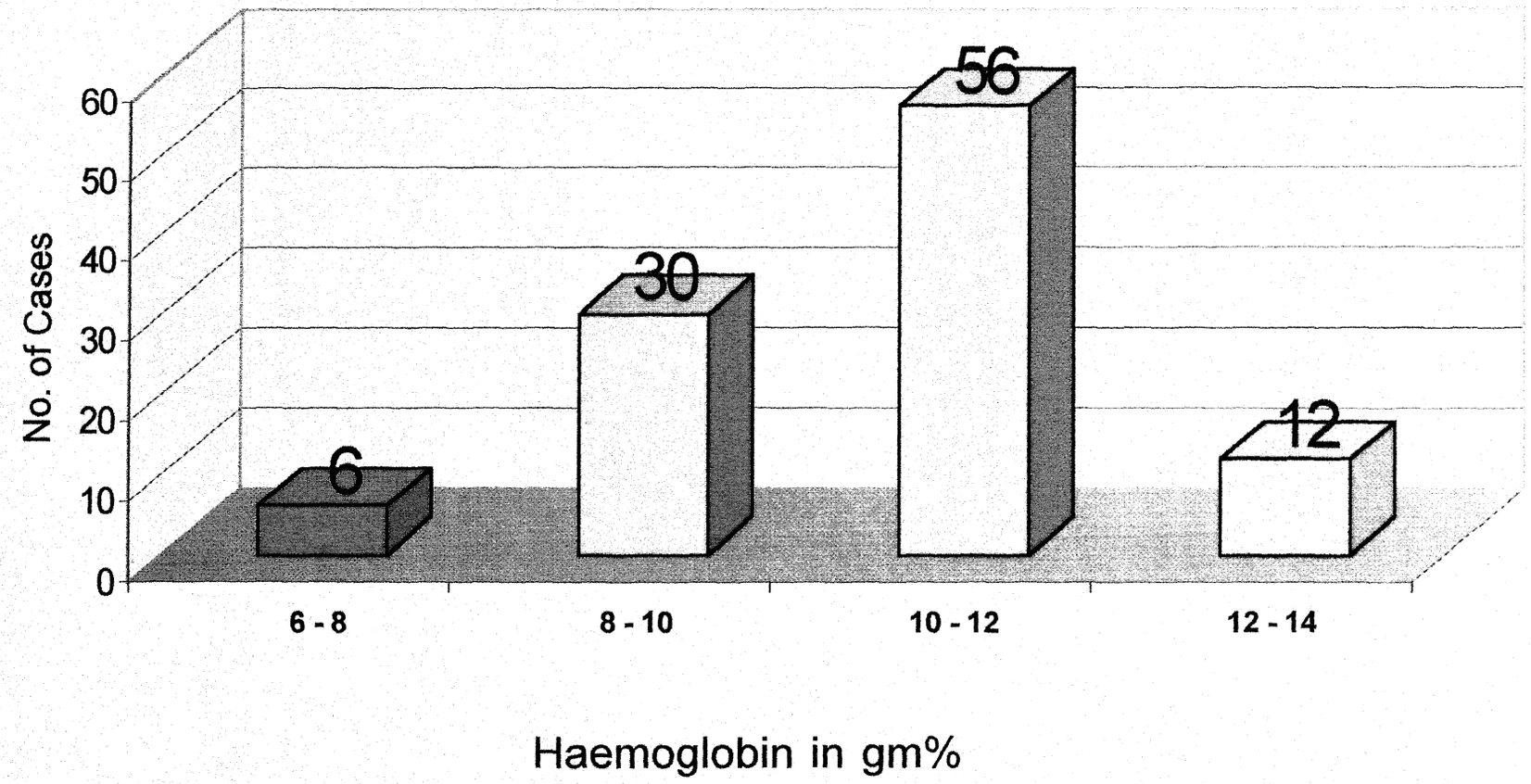
Clinical Staging of Disease :

Table 10 : Showing Clinical Stages of Disease

Age Group In Years	Total No. of Patients	Stage I		Stage II		Stage III	
		No.	%	No.	%	No.	%
11-20	15	8	53%	5	33%	2	13%
21-30	55	14	25%	28	50.9%	13	23.6%
31-40	20	8	40%	8	40%	4	20%
41-50	10	3	30%	4	40%	3	30%
51-60	2	-	-	-	-	2	100%
61-70	2	-	-	-	-	2	100%
Total	104	33	31.7%	45	43.2%	26	25%

33 cases (31.7%) were found in Stage I at the scale of clinical staging of disease while 45 cases (43.2%) were in Stage II and rest 26 cases (25%) were found in Stage III. 8 Cases (53%) of 11-20 age group were in Stage I while 5 cases (33%) were in Stage II

Bar Diagram No. 10 Showing Haemoglobin Percentage in the disease



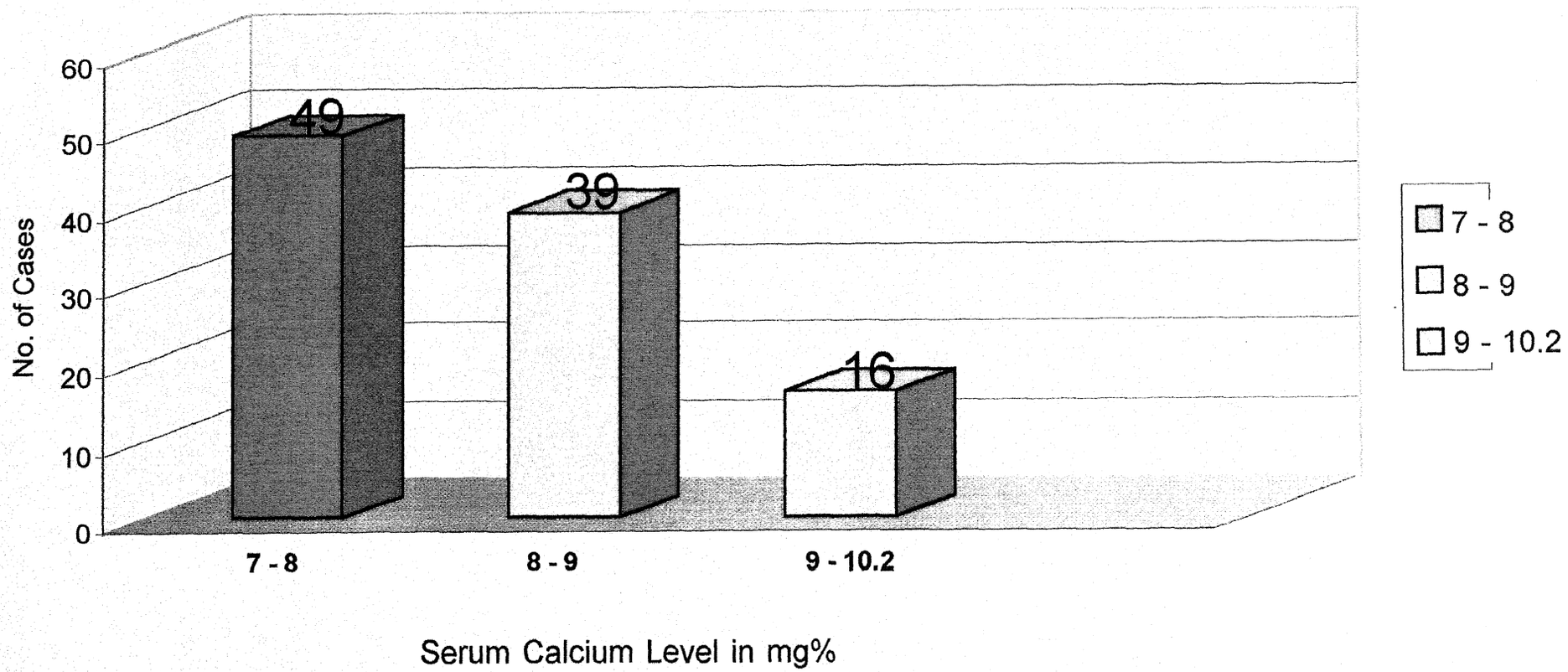
and 2 cases (13%) were in Stage III. In Age Group of 21-30, 14 cases (25%) were in stage I, 28 cases (50.9%) were in Stage II and 13 cases (13.6%) were in Stage III. In Age Group 31-40 years 8 case (40%) were in Stage I, 8 cases (40%) in Stage II and 4 cases (20%) in Stage III. In age group of 41-50 3 cases (30%) were in Stage I, 4 cases (40%) were in Stage II and only 3 cases (30%) were found in Stage III. Age Group 51-60 2 cases (100%) in Stage III and 61-70 age group 2 cases (100%) reported in Stage III.

Investigations :

Table : 11 Showing Haemoglobin Percentage in Various Age Group

Age Group In Years	Total No. of Patients	Haemoglobin in gm %							
		6 - 8		8 – 10		10 – 12		12 - 14	
		No.	%	No.	%	No.	%	No.	%
11-20	15	-	-	3	20%	10	66.6%	2	13.3%
21-30	55	2	3.6%	15	27%	30	54.5%	8	14.5%
31-40	20	2	10%	7	35%	9	45%	2	10%
41-50	10	-	-	3	30%	7	70%	-	-
51-60	2	1	50%	1	50%	-	-	-	-
61-70	2	1	50%	1	50%	-	-	-	-
Total	104	6	5.76%	30	28.8%	56	53.8%	12	11.5%

Bar Diagram No. 12 Showing Total Serum Clacium In the disease



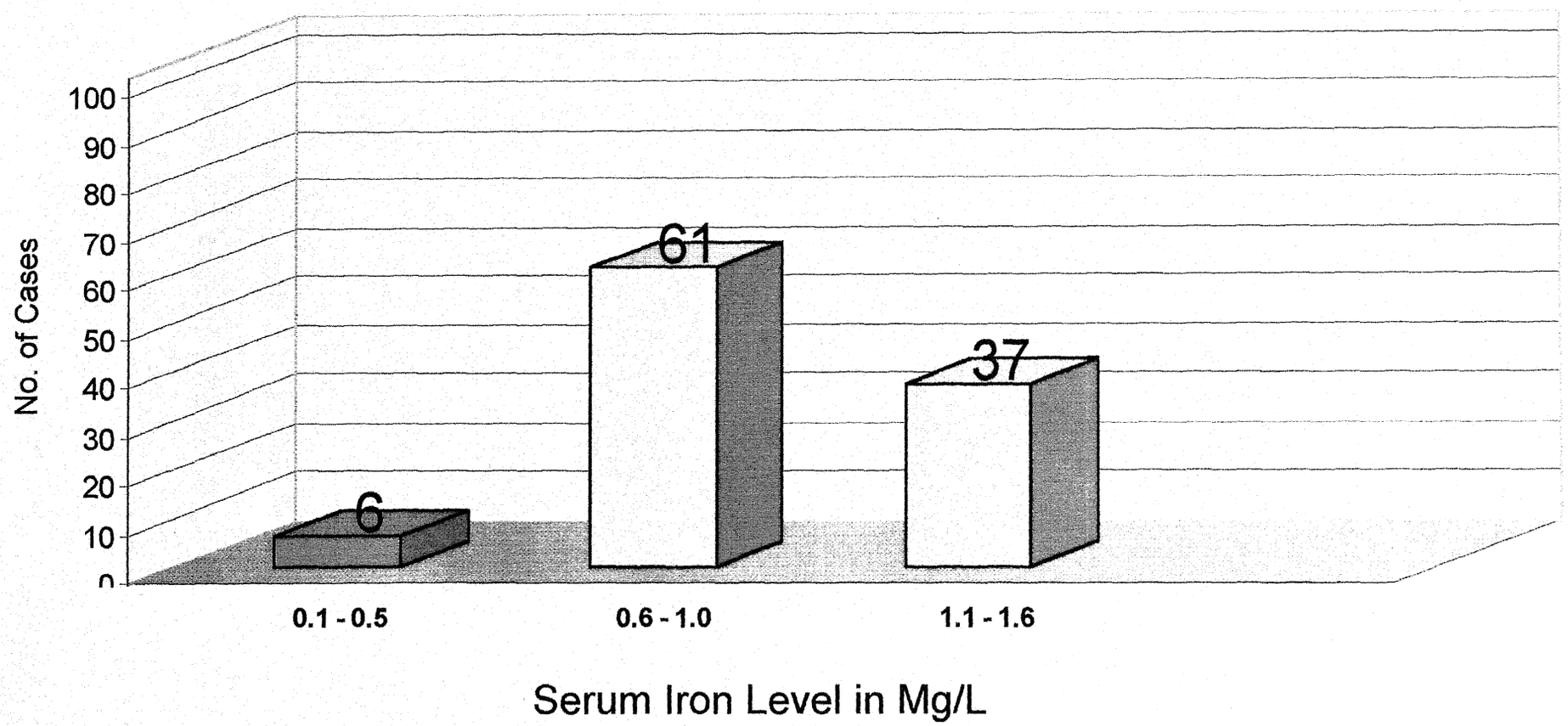
Out of 104 patient 6 cases (5.76%) had haemoglobin in range 6.0 to 8.0 gm%, 30 cases (28.8%) had haemoglobin in the range of 8.0 to 10 gm%, 56 cases (53.8%) had haemoglobin in the range of 10. To 12 gm% and 12 cases (11.5%) had haemoglobinh more than 12gm%. In both control and study group most of the patient (53.8%) had haemoglobin in the range of 10 to 12 gm%.

Table 12 : Showing Total Serum Calcium in Various Age Group

Age Group In Years	Total No. Of Patients	Serum Calcium In Mg %					
		7 – 8		8 – 9		9 – 10.2	
11-20	15	5	33.3%	7	46.6%	3	20%
21-30	55	29	29.57%	18	32.7%	8	14.5%
31-40	20	8	40%	10	50%	2	10%
41-50	10	3	30%	4	40%	3	30%
51-60	2	2	100%	-	-	-	-
61-70	2	2	100%	-	-	-	-
Total	104	49	47.1%	39	37.5%	16	15.38%

Out of 104 patients 49 cases (47.1%) had serum calcium 7-8 mg% (normal value - 8.8 to 10.2 mg%). 39 cases (37.5%) had serum calcium 8 to 9 mg% and 16 cases (15.38%) had serum calcium in the range of 9 to 10.2mg%. Age Group 11-20 5 cases (33.3%) had serum calcium 7 to 8 mg%, 7 cases (46.6%) had serum calcium 8 to 9 mg% and 3 cases (20%) were in range of 9 to 10.2mg%. In Age Group 21 to 30, 29 cases (52.7%) had serum calcium 7 to 8 mg%, 18 cases (32.7%) were in the range of 8

Bar Diagram No. 11 Showing Serum Iron Level in the disease

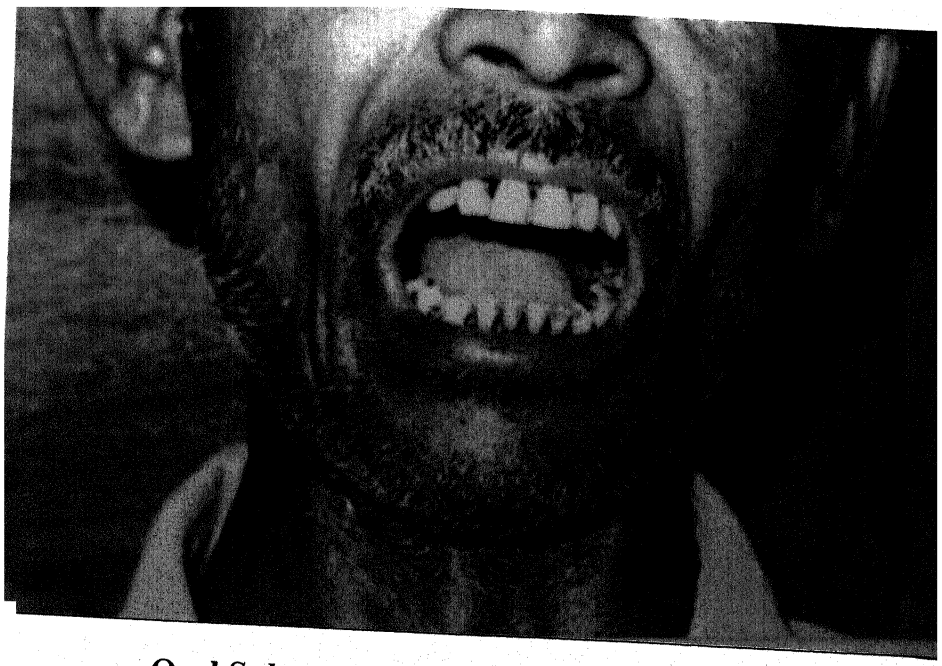


to 9 mg% while 8 cases (14.5%) had serum calcium in the range of 9 to 102mg%. In the Age Group of 31 to 10 8 cases (40%) had serum calcium 7 to 8mg%, 10 cases (50%) 8 to 9 mg% and 2 cases (10%) 9 to 10.2 mg%. In Age Group 41 to 50 3 cases (30%) had serum calcium 7 to 8 mg%, 4 cases (40%) had serum calcium 8 to 9 mg% and only 3 cases (30%) were in the range of 9 to 10.2 mg%. In age group of 51 to 60 and 61 to 70 all cases (4 cases, 100%) had serum calcium 7 to 8mg%.

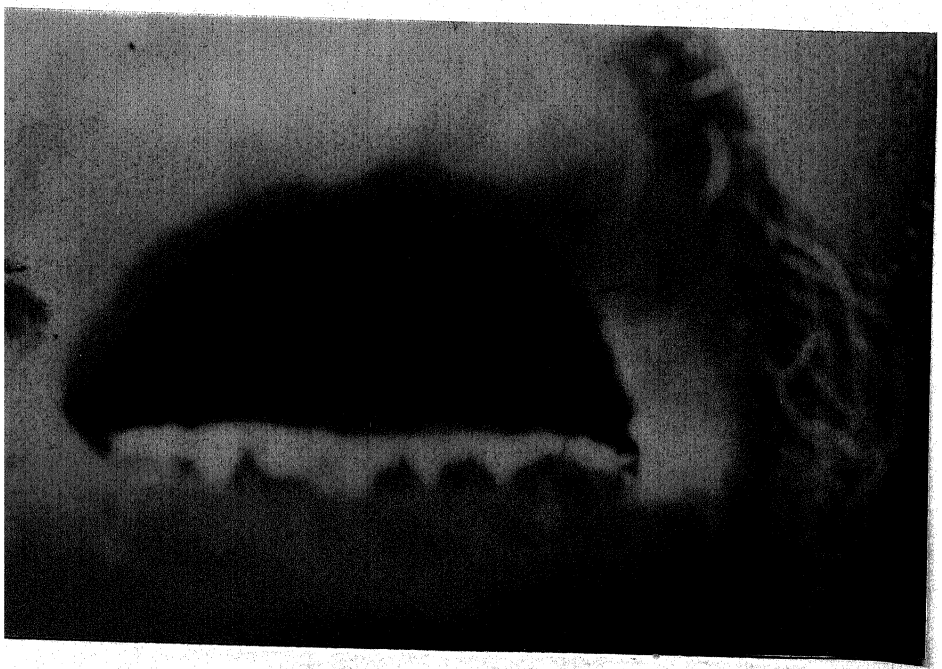
Table 13 : Showing Serum Iron Level in Mg / L.

Age Group In Years	Total No. of Patients	Serum Iron in Mg / L					
		0.1 – 0.5		0.6 – 1.0		1.1 – 1.6	
11-20	15	-	-	11	73.3%	6	26.7%
21-30	55	2	3.6%	32	58%	21	38%
31-40	20	2	10.%	10	50%	8	40%
41-50	10	-	-	6	60%	4	40%
51-60	2	1	50%	1	50%	-	-
61-70	2	1	50%	1	50%	-	-
Total	104	6	5.7%	61	58.6%	37	35.5%

Out of 104 patients 6 cases (5.7%) had Serum Iron less than 0.5mg/L, 61 cases (58.6%) had serum iron 0.6 to 1.0 mg/L, 37 cases (35.5%) had serum iron in the range of 1.1 to 1.6 mg/L. In the age group of 11-20 years 11 cases (73.3%) had serum iron 0.6 to 1.0 mg/L, 4 cases (26.7%) had serum iron 1.1 to 1.6mg/L. In the age group 21 – 30 years 2 cases (3.6%) had serum iron less than 0.5 mg/L, 32 cases (58%) had serum iron 0.6 to 1.0 mg/L and 21 cases (38%) had serum iron 1.1 to 1.6 mg/L. In the Age



Oral Submucous Fibrosis in an old male



Oral Cancer with Oral Submucous Fibrosis

Group of 31 – 40 years 2 cases (10%) had serum iron less than 0.5mg/L, 10 cases (50%) had serum iron 0.6 to 1.0mg/L and only 8 cases (40%) had serum iron 1.1 to 1.6mg/L. In the Age group of 41 – 50 years 6 cases (60%) had serum iron 0.6 to 1.0 mg/L, 4 cases (40%) were in range of 1.1 to 1.6mg/L. In the age group of 51 – 60 and 61 – 70 years both have 1 cases (50%) serum iron less than 0.5mg/L, 1 cases (50%) had serum iron in the range of 0.6 to 1.0mg/L. In this age group .

Table 14 : Showing Oral Cancer and Malignant Transformation in the Disease.

Total No. of Cases	Total Malignant		Coexistence of Malignancy & OSMF		Malignant Transformation	
	No	%	No	%	No	%
104	5	4.8%	3	2.8%	2	1.92%

Out of 104 cases 5 cases (4.8%) were diagnosed as carcinoma of oral cavity. In this study Coexistence of Malignancy & Oral Submucous Fibrosis were found in 3 cases (2.8%) and malignant transformation rate were considered together.

Treatment:

To evaluate role of calcium and iron in treatment of the disease patient were divided into two groups, Control group 52 cases (50%) and Study group 52 cases (50%). Patient were assessed for improvement in symptoms. Finally over all result of both therapy were taken into consideration

Bar Diagram No. 13 Showing Result in Both Control & Study group

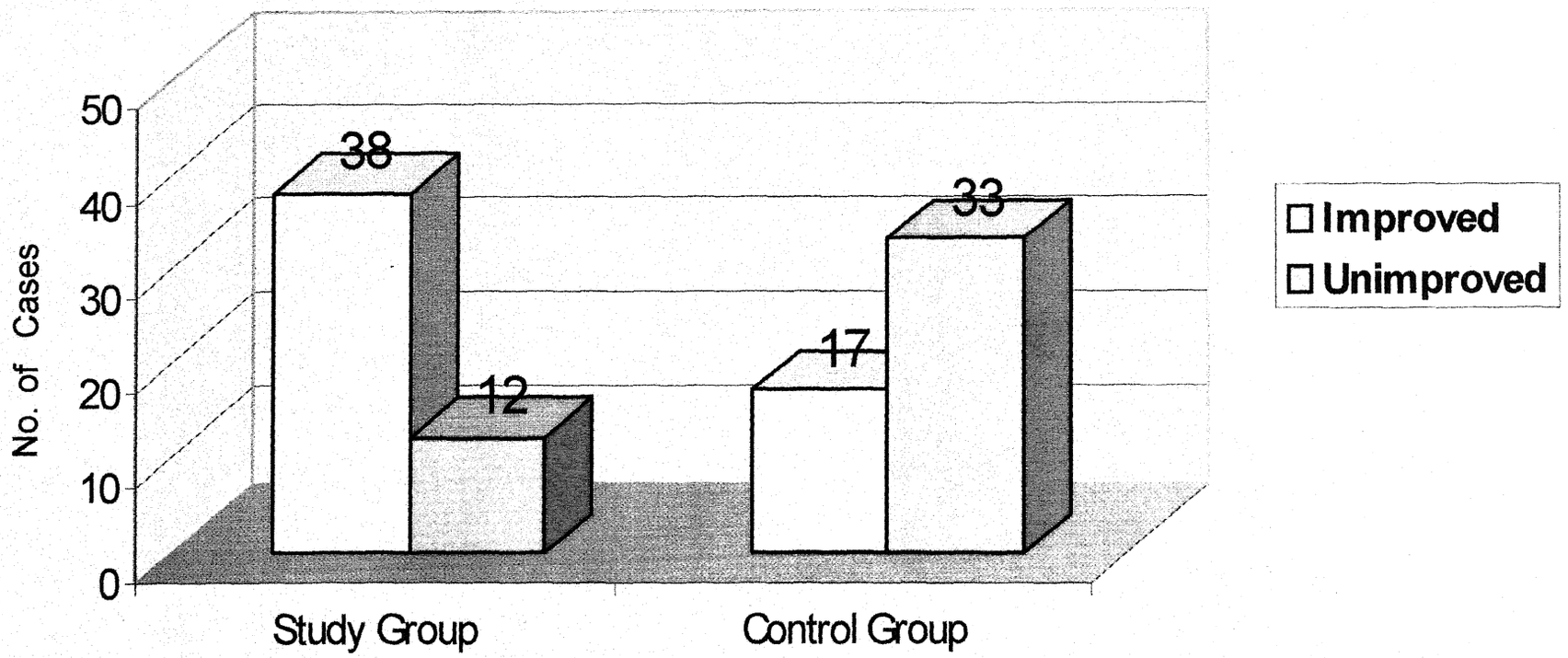


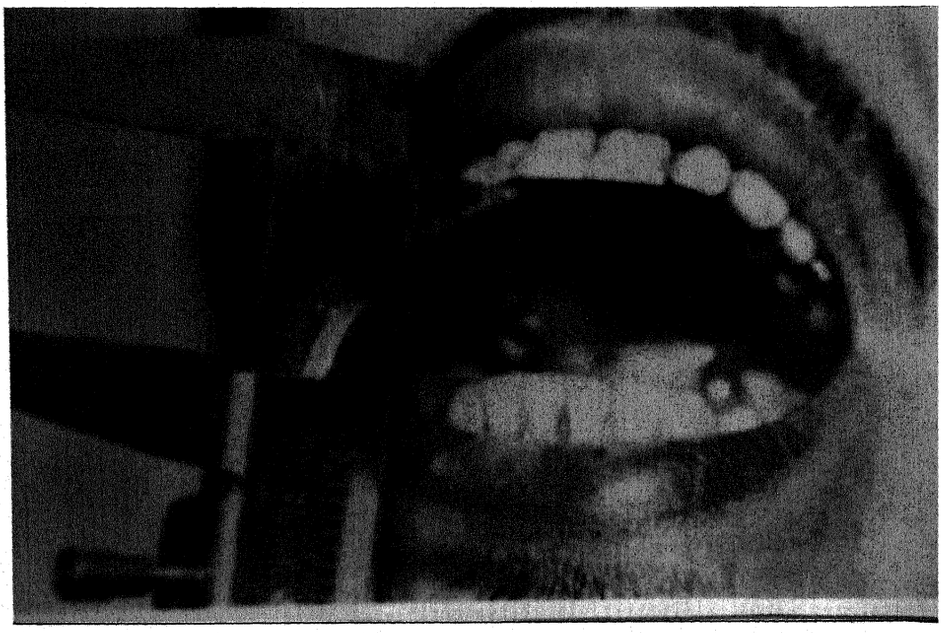
Table 15 : Showing Result of treatment in both control and study group.

Treatment	No. of Cases	Improved		Unimproved	
		No.	%	No.	%
Control Group	52	17	32.6%	33	63.46%
Study Group	52	38	73%	12	23%
Total	104	55	52.8%	45	43.2%

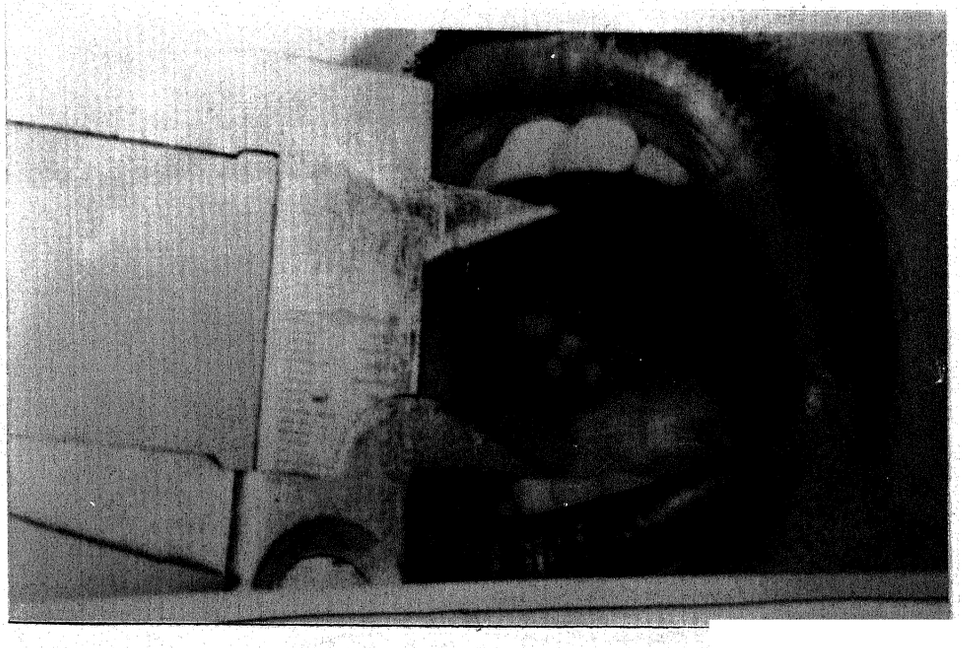
In control group 52 cases (50%), there were improvement in symptoms in 17 cases (32.6%) while unimproved or detoriate cases were 33 (63.46%). In Study group 52cases (50%) there were improvement in symptoms in38 cases (73%) while 12 cases (23%) not respond to the treatment.

Table – 16 : Showing Post treatment relief in symptoms in the disease.

S.No	Symptoms	Control Group	Study Group	Total Cases	Percentage
1.	Difficulty to open mouth.	17	38	55	52.8%
2.	Intolerance to Hot & a spicy food	17	38	55	52.8%
3.	Inability to protrude tongue	8	32	40	38.4%
4.	Nasal Voice	4	11	15	14.42%
5.	Inability to whistle	3	9	12	11.5%
6.	Decrease in taste Sensation	6	20	26	25%



Trismus before treatment



Trismus after treatment

Management of Failure Cases :

Table –17 : Showing post treatment trismus in control & study group.

Groups	Interincisor Mean trismus (cm)	Distance Post treatment Trismus (cm)	Mean Relief in trismus (cm)
Control	2.25	2.62	0.37
Study	2.15	3.62	1.47

45 Cases were observed from Both Groups of treatment. 5 Cases are diagnosed as malignancy of Oral Cavity, leaving 40 failure cases of Oral Submucous Fibrosis (Control Group – 33 cases, Study Group – 12 cases). These 40 cases were treated with combination of local Hydrocortisone, vitamins supplementation and antioxidants etc. 37 cases (82.2%) respond to the treatment while 8 cases (17.7%) did not respond to any treatment.

Table 18 : Showing result of management of failure cases.

Total No. of Patient	Improved		Unimproved	
	No.	%	No.	%
45	37	82.2%	8	17.7%

DISCUSSION

Discussion

The present observation included 104 cases who attended out door of the Department of Otolaryngology, of M. L. B. Medical College JHANSI. (U.P.)

Prevalence

The prevalence (Table 1) of Oral Submucous Fibrosis in this region was found 1.81%. Pindborg et al. (1964), during epidemiological survey, found average prevalence of Oral Submucous fibrosis, 0.5% which ranged from 0.18% to 1.22%. In their survey prevalence at Lucknow was 0.51%.

Age :

Average age in this observation was 26.2 years. Most of the patients were reported (Table 2) from the 2nd, 3rd & 4th decades (14.42%, 52.88% and 19.23%). The patients of these three decades shared 90 (86.53%) in 104 observed cases. Sirsat and Khanolkar (1962) studied age distribution in Oral Submucous Fibrosis in patients in Bombay City found that majority of the patients were belonging to age group of 21-40 years. Similar observations also were made by Pindborg et al. (1964).

Sex :

Sex distribution (Table 3) showed male predominance in the observed sample. Share of male patient was 84 (80.74%) and of female patient was 20 (19.22%). Sex trend did not show any definite trend during epidemiological surveys of Pindborg et

al. (1964) while Rao (1954), Wahi (1966) and Gupta (1978) observed female predominance of the disease. Sirsat and Khanolkar (1966), in series of studies could not conclude a definite sex trend of the disease. In few series it was female dominating while other series showed male predominance.

Religion :

Religious trend of oral submucous fibrosis (Table 4) pointed its incidence 80.76% in Hindus, 15.38% in Muslims and 3.8% in other (Christians). Sirsat and Khanolkar (1962) observed that no caste in particular and no religion was specially affected by this disease. They also indicated that caste and community trend of the disease depend upon the location of the hospital where observation is being made. In epidemiological surveys, Pindborg et al. (1964) found that none of the caste and community is specially affected. The disease is evenly distributed in all castes in different communities was similar to the distribution of their population in the society. The disease was found evenly distributed in all communities, in relation to their population.

Rural/Urban :

The disease prevalence (Table 5) in rural and urban cases was 42.30% and 57.69% respectively. From the very first observation made by Schwartz (1952) it was found that rural and urban, both populations are equally affected by oral submucous fibrosis. The similar inference were made by Sirsat and Khanolkar (1962), Pindborg

et al (1964) and Wahi (1966). In present study the earlier age groups were dominated by urban patients while the rural patients were dominating in the later age groups. It is particularly due to awareness of the disease in advanced and educated societies.

Social Stages :

All social classes were affected with this disease (Table 6). Major share of the disease came from the class III and class IV 40 (38.46%) and 41 (39.42%) cases respectively. Paymaster (1956), Pindborg et al. (1964), Rao (1962), Sirsat & Khanolkar (1962) and Lay (1982) concluded the incidence of oral submucous fibrosis in all social classes. Our community and social setup is dominated by class IV and class III population. Therefore large share of patients came from these two classes of society.

Clinical Presentation :

Su (1954), DeSa (1957) described inability to open mouth being the commonest presentation of the disease. Later statements of the workers also supported the views made by Su and DeSa. Paymaster (1957) and Pindborg et al. (1964) found intolerance to hot spicy foods and chilies (burning sensation) as the earliest symptom but it was inability to open mouth, which brought the patients to the clinicians. Paymaster (1957) and Rao (1962) described inability to protrude tongue as third commonest symptom of oral submucous fibrosis. Rao pointed that, as the disease becomes advanced, pain and swelling around lower jaw resulted. All four symptoms made the eating of spicy food

both painful and difficult, Pindborg et al. (1964). Rao (1962) found carache associated with oral submucous fibrosis. He explained its occurrence possibly due to involvement of opening of Eustachian tube into oropharynx. Extensive fibrosis of palate lead to nasal voice and nasal regurgitation (Sirsat and Khanolkar, 1966). Paymaster (1957) and Rao (1962) indicated that involvement of buccal mucosa made it, luster less and the patient became unable to blow a candle out or unable to whistle. Soni (1978) observed loss of taste sensation in advanced cases of oral submucous fibrosis.

In this observation the chief complaints were difficulty to open mouth in 85.5% (89) cases, intolerance to hot and spicy foods in 81.7% (85) cases, inability to protrude tongue in 38.46% (40) cases, pain and swelling around jaw and neck in 2.8% (3) cases . Among other associated symptoms the earache was presented in 2.8% (3) cases and loss/decrease in taste sensation in 25.00% (26) cases. 11.5% (12) cases showed inability to whistle. Nasal voice and nasal regurgitation was observed in 14.42% cases and 2.8% cases respectively.

Difficulty to open mouth and intolerance to hot and spicy food was evenly observed in all age groups where as inability to protrude tongue and pain and swelling around lower jaw is presented by the patients of more advanced age. These two symptoms were directly related to the severity of the disease. Nasal voice and nasal

regurgitation too, were related to the severity of the disease while age and severity of the disease both, were related to the decrease in taste sensation (Table 7).

Personal Habits :

Tobacco Chewing :

90% (94) cases were tobacco chewers. Incidence of tobacco chewing increased with increasing the age. The highest percentage of tobacco chewing was in later age groups which was equally practiced in rural and urban population. Pindborg et al. (1964) found tobacco chewing in most of the patients, suffering from oral submucous fibrosis. Wahi and Kapoor (1966) also confirm the observations of Pindborg. They observed tobacco chewing in 40% cases of this disease. Moos (1968) indicated tobacco, one of the commonest irritating material to oral cavity (Table 8).

Examination :

Trismus :

Most of the cases were reported with trismus from stage I, (31.7%) and stage II (43.2%). Incidence of trismus was evenly distributed in all age groups. Su (1954) and DeSa (1957) described trismus as the commonest symptoms of the disease. In their observations, they found trismus in 60% and 70% cases respectively (Table 10).

Site of Oral Submucous Fibrosis:

Sirsat and Khanolkar (1962) found severe fibrosis of palate in 80% cases of oral submucous fibrosis. Similar observations were made by Pindborg et al. (1964). They

found fibrosis of cheek in 75% cases. Rao (1964) observed the distribution of fibrotic bands in oral cavity and found that palate and cheeks were mainly affected. In his observation fibrosis of palate and cheek was followed by fibrosis of pillars and tongue. Uvula, lip and Pharynx were less affected sites of fibrosis.

In present observation palatal fibrosis was found in 91% (95) cases. Fibrosis of cheek was also presented in 93% (97) cases. Fibrosis of tongue was seen in 68% (71) cases while the fibrosis of retromolartrigone were seen in 88% (92) cases. As the disease advanced, more area of the oral cavity were affected. The findings of Rao (1964) were similar to the findings mentioned above (Table 9).

Ankyloglossis:

Ankyloglossis was observed in 38.46% (40) cases. The ankyloglossic symptoms were related to severity of the disease and extent of the fibrosis. In present observation, this symptom was presented by Mosy of the case of 2nd and 3rd stage of the disease, Rao (1962) found ankyloglossia when the fibrosis occurred with the involvement of tongue muscles. Ankyloglossia is resulted in most of the advanced cases of oral submucous Fibrosis, Rao (1962) and Pindborg et al. (1964) (Table 7).

Clinical Staging :

De Sa (1957) classified disease into three stage. His classification was entirely based upon the extent of fibrosis and severity of the disease. Pindborg et al. (1964) observed that rural patients usually came in advanced stages. In present observation

25% (26) cases were observed in stage III, 43.2% (45) cases in stage II and 31.7% (33) cases in stage I. Rural and old aged patients were in stage II and III of the disease (Table 10).

Investigation :

Anaemia :

5.76% (6) cases were having haemoglobin less than 8 gm% and 28.8% (30) cases were having haemoglobin in the range of 8-10gm% (Table 11). These cases were poorly nourished. The incidence of anaemic cases increased with the age. Rural patients were more anaemic than the urban. Sirsat and Khanolkar (1962) observed nutritional deficiency anaemia in one third cases of oral submucous fibrosis in Bombay City. Pindborg et al. (1964), in their epidemiological survey, found poor nutritional status and aneamia in rural population. Later workers, Mukherjee and Biswas (1972) also confirmed the findings of previous workers.

Serum Calcium :

In the present observation 47.1% (49) cases had serum calcium in the range of 7-8 mg% while 37.5% (39) cases had serum calcium in the range of 8-9 mg% and 15.38% (16) cases were having serum calcium in the range of 9-10.2mg%. The decreased serum calcium level was related to severity of disease and extent of the fibrosis. As the disease and age advanced the serum calcium level decreased (Table 12).

Serum Iron :

Paul RR, Chattererjee J, Das AK, Dutta SK and Roy D (1996), Anuradha CD, Shyamala Devi CS (1993) and Rajendran R, Vasudevan DM and Vijay Kumar T (1990). Observed significant decrease in Serum Iron. In present study 5.7% (6) cases had serum iron less than 0.5mg/L 58.6% (61) cases had serum iron in the range of 0.6

to 1.0 mg/L (Table 13). Decreased Serum Iron was directly related to extent of disease and age of patients.

Oral Cancer & Malignant Transformation :

Paymaster (1957) first indicated the incidence of oral cancers with oral submucous fibrosis. Pindborg et al. (1964) observed incidence of oral cancers in oral submucous fibrosis as 1.5%. other workers, Rao (1962), Wahi and Kapoor (1966) also found increasing incidence of oral cancers in oral submucous fibrosis as compared to its incidence in normal individuals. Murti (1985) observed 7.5% incidence of co-existence of oral cancer and oral submucous fibrosis. In his observation malignant transformation rate was 4.5%.

In present study (Table 14) the incidence of oral cancer in oral submucous fibrosis was found in 4.8% (5) cases. The malignant transformation rate in the present sample was found 1.92%.

Treatment :

Sirsat and Khanolkar (1962) advocated vitamin supplementation in the management of the disease. They found remission of symptoms in 40% cases of oral submucous fibrosis. They observed that less severe symptoms were improved easily this treatment and it was very effective in early stages of the disease process. They put their views forward, keeping the fact that most of the cases reported in their observations were anaemic and nutritionally poor, into mind. They advocated systemic and local supplementation of vitamins B complex, A & E. Local treatment consisted of intra oral injections of vitamin A & E. Varghese (1987) observed reduction of serum zinc level in the patients suffering from oral submucous fibrosis. Paul RR, Chattejee J, Das Ak, Dutta Sk, Roy D (1996) found that decreased serum zinc and iron can be regarded as an alternate indicator of the precancerous nature of Oral Submucous Fibrosis. Maher R, Aga P, Johnson NW (1997) found significant improvement in symptoms of Oral Submucous Fibrosis after supplementation with

multivitamins (Vit. A, B, C, D & E) and minerals (Iron, Calcium, Copper, Zinc & Magnesium etc.).

In a preliminary study of serum protein, Ascorbic Acid, iron & tissue Collagen in Oral Submucous Fibrosis, CD Anuradha & CS Shyamala Devi (1993), found that Ascorbate and Iron levels decreased perhaps because of their utilization in collagen synthesis.

Quantitative analysis of human buccal epithelium in Iron deficiency Anaemia ,JS Rennie, DG Mac Donald (1982) found that buccal epithelium is significant thinner than normal and this reduced epithelial thickness is due to a reduction in the thickness of the maturation compartment.

Serum levels of Iron and proteins shows significant decrease in Oral Submucous Fibrosis, Rajendran R, Vasudevan DM, Vijay Kumar T (1990). Taking this fact into consideration, patients of the present sample of study were supplemented with oral calcium and iron.

Result :

In present study result comparison of both groups (Study Group 52, Control Group 52) showed improvement in 52.8% (55) cases. 32.6% (17) cases in Control group and 73% (38) cases in Study group (Table 15).

Management of Failure Cases:

Kaker (1985), Sinha (1980) compared Hylase, hydrocortisone and combination of these two and obtained best response with the combined treatment.

In the present study 45 failure cases of both groups, 63.46% (33) cases in Control Group and 23% (12) cases in Study groups, were subjected to combined treatment of local hyaluronidase, Hydrocortisone and vitamins supplementation with antioxidants etc. 82% (37) cases respond to the treatment and showed improvement in Symptoms 17.7% (8) cases remained unimproved, 5 cases of these were diagnosed malignancy of oral cavity and not respond to the treatment.

SUMMARY & CONCLUSIONS

Summary & Conclusions

The present study was based over observations on 104 cases of oral submucous fibrosis, attending out patient department of ENT, M. L. B. Medical College, Jhansi, Bundelkhand region (U.P.) Detailed history of the patients were recorded with special consideration of the food habit and personal history to detect the causative factors of the disease. The cases were thoroughly examined and investigated clinically. The patients were divided into two groups (Control & Study) for the purpose of evaluation of the management and improvement. The conclusions drawn from this study are :

1. *The prevalence of oral submucous fibrosis in this region is 1.81%.*
2. *The incidence of disease was more in 2nd, 3rd and 4th decades of age. Average age was 26.2 years. Sex distribution showed male predominance (4 males : 1 female) in the observed sample. Casts and religious distribution did not indicate any definite trend. The disease affected the patients of all social status and evenly shared by all economic groups, rural and urban societies.*
3. *The important aetiological factors lies in the personal habits of the patients. 90% (94) cases were habitual of tobacco chewing. In present observation.Pan Masala, a new irritant was emerging as a factor in the aetiology of the disease. Especially, in young and urban population, it is an important aetilogical factor.*
4. *The disease presented with intolerance to hot and spicy foods in 81.7% (85) cases, difficulty to open mouth in 85.5% (89) cases, inability to protrude tongue in 38.46% (40) cases and pain and swelling around jaw and neck in 2.8% (3) cases. Among other associated symptoms, earache was presented in 2.8% (3) cases. Loss/Decrease in taste sensation was complained by 25% (26) cases.*

The cases of the present study, unable to whistle were 11.5% (12) while 14.42% (15) cases showed nasal voice and 2.8% (3) cases, nasal regurgitation. Inability to open mouth and intolerance to chilies and hot spicy foods were the complaints equally presented in all age groups whereas ankyloglossia and swelling and pain around lower jaw was presented in the advance aged patients and in severe stage of the disease. Nasal Voice and nasal regurgitation was presented in severe cases of palatal fibrosis.

5. *Palatal fibrosis was observed in 91% (95) cases and fibrosis of cheek each was observed in 93% (97) cases and involvement of tongue in 68% (71) cases. Severity of these observations was related to the severity of the disease. Retromolartrigone were the third commonest site where fibrosis occurred (88%, 92 cases). The fibrosis of cheek, palate tongue and retromolartrigone resulted trismus, the fibrosis of tongue produced ankyloglossia while the fibrosis of palate and uvula resulted in nasal voice and nasal regurgitation. Pharyngeal fibrosis produced earache and hard of hearing, even deafness. Patients of old age and of nutritionally poor built, usually presented these symptoms. Taste papillae were lost due to fibrosis and the tongue became smooth which resulted impairment in taste sensation 25% (26) cases.*

6. *On the scale of clinical staging 31.7% (33) cases were in stage I, 43.2% (45) cases in stage II and 25% (26) cases in stage III.*

7. *Investigative procedure revealed haemoglobin less than 8gm% in 5.76% (6) cases. Haemoglobin in the range of 8-10mg% 28.8% (30), haemoglobin in the range of 10-12gm% 53.8% (56) cases. Only 11.5% (12) cases had haemoglobin more than 12gm%.*

Serum calcium was found less than 8mg% in 47.1% (49) cases and in the range of 8-9mg% in 37.5% (39) cases. Only 15.38% (16)cases had serum calcium in the range of 9-10.2mg%.

Serum Iron was found less than 0.5mg/L in 5.7% (6) cases and in the range of 0.6-1.0mg/L in 58.6% (61) cases while only 35.5% (37) cases had serum iron in the range of 1.1-1.6mg/L.

8. *Co-existence of oral cancer and oral submucous fibrosis was found in 2.8% (3) cases.*

9. *Malignant transformation rate in the present sample was 1.92%. the malignant transformation in oral submucous fibrosis indicate the precancerous nature of the disease.*

10. *It seems that the decreased level of Serum Iron & Serum Calcium may be because of their utilization in collagen synthesis and reduction of the thickness of maturation compartment of buccal epithelium in Oral Submucous Fibrosis.*

11. *The decreased Serum Calcium level was related to severity of disease and extent of Fibrosis.*

12. *The decreased level of Serum Iron & Serum Calcium can be regarded as alternate indicator of the precancerous nature of Oral Submucous Fibrosis.*

13. *Oral calcium and iron supplementation showed fast and better improvement in symptoms as compared to the conventional treatment*

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